Nutrition and Cognition:

Exploring their Relationship from Two Sides of the Same Coin

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

Part 1: This thesis begins with a literature review of the evidence base of the neuropsychological profile of adolescents with anorexia nervosa (AN). A systemic review identified 36 relevant studies. Results indicated inconsistent findings across studies throughout each neuropsychological domain under review, such as some finding set-shifting difficulties in some young people with AN while others did not find any differences in performance. Adolescents with AN typically performed within the average range, with many studies not finding any significant differences between their performance and healthy adolescents' performance. Performance often improved following weight-gain. Drawing firm conclusions about these findings was hampered by methodological and task differences between the studies. Future research should endeavour to take into account the potential impact of confounding variables, such as co-morbid diagnoses and psychoactive medication, on outcome measures in this population.

Part 2: The empirical paper reports the results of a joint study that investigated the effects of intermittent fasting in healthy adults, using the 5:2 diet. This within-subjects study explored the differences in performance on fasting versus non-fasting days, on a series of cognitive tasks. The results indicated no significant differences between fasting and non-fasting days on any task administered. This suggests there are no detectable effects of the 5:2 diet on the cognitive domains assessed over a brief time period. These findings do not replicate the results found in acute fasting studies, but are more in line with those reported from other dieting strategies.

Part 3: Finally, the critical appraisal offers some reflections on the whole research process. It emphasises the need for different methodologies to tackle the complex problem of understanding and treating eating disorders. It also considers the benefits of the scientist-practitioner model.

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Part 1: The Literature Review

The Neuropsychological Profile of Anorexia Nervosa in Adolescence: A Systematic review

Abstract

Aims

No recently published reviews of research specifically regarding the broad neuropsychological profile of adolescents with anorexia nervosa (AN) exist, despite the growth in research in this area in the past decade. This systematic review aims to synthesise and critique the available evidence concerning the neuropsychological profile of adolescents with AN under a range of cognitive domains, to better inform researchers and practitioners working in the field. Experts in the field have argued that a deeper understanding of the neuropsychological profile of adolescents with AN will better inform etiological and treatment models.

Methodology

A systematic search was carried out in six electronic databases, Web of Science, Scopus, Pub Med, Science Direct, Embase and PsychInfo. Search terms relating to AN, combined with neuropsychology and adolescence were used, yielding 5470 results. Of these, 36 studies met the inclusion and exclusion criteria, and were quality ranked using pre-defined criteria.

Results

An inconsistent picture emerged from the evidence base, given the wide variety of methodologies and tasks used to measure performance in the studies under review. A critical review of the evidence is presented in the following domains: intelligence, processing speed, attention, aspects of executive functioning (including inhibitory control, cognitive flexibility, decision-making, planning, central coherence, working

memory & verbal fluency), visuospatial abilities, verbal abilities, memory and academic abilities.

Conclusions

Despite the inconsistencies in results and methodologies, adolescents with AN displayed neuropsychological abilities that fell broadly within the average range, according to normative data. Differences between AN and healthy control group performances, where present, were subtle across tasks. It should also be noted that AN groups often outperformed psychiatric control groups. Future research should include adequate contextual detail regarding sample characteristics, as well as analysing the effects of potential confounding variables on outcome measures. There is no 'classic cognitive profile in adolescents with AN, and as such, the importance of individually tailored assessment and formulation is underlined.

Keywords

Anorexia Nervosa - Adolescents - Children - Neuropsychology - Cognition - Review

The Neuropsychological Profile of Anorexia Nervosa in Adolescence: A Systematic review

Anorexia nervosa (AN) may be a relatively rare mental health condition in the general population, but given the high rates of mortality and morbidity associated with it (Arcelus, Mitchell, Wales, and Nielsen (2011); (Hoek, 2006), this condition requires significant clinical attention. In adolescence, the lifetime prevalence of AN has been estimated to be around 0.3% using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) criteria, (Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011), with higher rates of 1.7 % being reported using DSM 5 criteria (Smink, Hoeken, Oldehinkel, & Hoek, 2014). One meta-analytic review reported an averaged crude mortality rate of 5% at four to ten year follow-ups, with less than one half of patients considered recovered, one third improving and one fifth remaining chronically ill on average (Steinhausen, 2002). The typical duration of AN in community samples has been measured at 3.4 years (Wentz, Gillberg, Anckarsäter, Gillberg, & Råstam, 2009).

According to the criteria set out in DSM 5 (American Psychiatric Association, 2013), to be diagnosed with AN, individuals must display:

- Persistent restriction of energy intake leading to significantly low body weight (in the context of what is minimally expected for age, sex, developmental trajectory, and physical health).
- Either an intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain (even though of significantly low weight).
- Disturbance in the way one's body weight or shape is experienced, undue influence of body shape and weight on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Smink, Van Hoeken, and Hoek (2012) concluded, following a review of recent epidemiological studies, that AN is relatively common among young women. While prevalence rates have remained relatively stable over previous decades, they detected a rise in incidence amongst the high-risk group of 15-19 year olds, for reasons as yet unclear. Researchers have also reported that the age of onset is decreasing over time (Favaro, Caregaro, Tenconi, Bosello, & Santonastaso, 2009), though AN typically has its onset in adolescence. This is worrying, as the transition from childhood to adolescence is a time of significant physical and cognitive development. It is the period during which puberty occurs, leading to significant physical changes, including those in the brain (Blakemore & Choudhury, 2006). Therefore, restrictions in eating leading to insufficient nutrient intake could have serious lifelong consequences for a young person (Bourre, 2006).

A better understanding of the factors that contribute to and maintain AN is needed given how difficult it is to treat and its high-levels of chronicity. Its ego-syntonic nature often leads to ambivalence about recovery. Treating AN as soon as possible is key, as researchers have advocated that effective treatment in adolescence can shorten the duration of common mental health conditions and prevent further morbidity in adulthood (Patton et al., 2014). With regard to AN, some experts have suggested that unless treatment is delivered within the initial few years after onset, poor outcomes are likely, with decreased effectiveness of therapy input after this period (Treasure & Russell, 2011). Indeed, higher recovery rates from AN are seen in adolescents, when compared to adults (Guarda, 2008). However, early detection is a challenge due to the secrecy associated with AN and the lack of recognition of the seriousness of the condition for those suffering from it, an inherent part of the condition.

Given that the aetiology of AN is complex, likely to be multi-factorial and not yet clearly understood, attention is increasingly turning to its pathophysiology and the use of neuroscientific approaches in AN research. It is hoped that this approach will bring about more effective treatments. It is now known that AN is more genetically heritable than previously thought (Bulik et al., 2006), representing a challenge to the sociocultural factor causes that have dominated discourses previously. Agrawal and Lask (2009) highlighted the valuable role neuropsychology has to play in understanding the neuroscience of eating disorders (ED). This potential has vastly increased following recent advances in neuroimaging. These advances have facilitated greater understanding of brain-behavior relationships by making more accurate and detailed information about neural structure available.

Neuropsychologists study brain-behaviour relationships by observing the brain's functioning through behavioural testing and relating this to knowledge about the structure of the brain (Heilbrun et al., 2003). Neuropsychology has a potentially valuable role in contributing to understanding the aetiological process in AN (Kidd & Steinglass, 2012). Researchers use specific behavioural tasks that have been standardised in the general population in order to measure various domains of cognitive functioning (Kidd & Steinglass, 2012). However, this area of research is underrepresented and has yet to have the same high level of impact as research into eating disorder scales and measurement; when looking at the top 100 cited papers in AN (Lipsman, Woodside, & Lozano, 2014). By better understanding the neuropsychological functioning of adolescents with AN, clinicians may be aided in identifying and developing therapies that will better promote recovery from this difficult to treat condition (Espie & Eisler, 2015). Indeed this process has already begun with the development of a new psychological therapy, cognitive remediation therapy (CRT) that

aims to improve neuropsychological functioning in order to promote recovery in individuals with AN (Tchanturia, Lloyd, & Lang, 2013).

In adults with AN, a distinct cognitive profile is emerging from the evidence base, including difficulties in aspects of executive functioning, specifically set-shifting, weak central coherence and visuospatial processing impairments (Rose, Davis, Frampton, & Lask, 2011). However, given the inherent difficulties in conducting research in this rare population and the different research designs and tasks employed (Tchanturia & Lang, 2015), the question of whether these observed neuropsychological profiles in AN are state (i.e. related to consequences of starvation) or trait related (i.e. pre-morbid characteristics) remains difficult to answer, as there are many contradictory findings reported in the literature. Some studies have reported improvements in cognitive functioning following recovery (e.g. Szmukler et al., 1992; Takano et al., 2001; Moser et al., 2003), while others have found specific impairments to persist, such as set-shifting (e.g. Roberts, Tchanturia, & Treasure, 2010), which have even been found in unaffected siblings (Tenconi et al., 2010). Previous reviews of the neuropsychological evidence base have highlighted the difficulties in drawing firm conclusions (Jauregui-Lobera, 2013). There is also the potential that the cognitive profiles observed are a scar of the disorder in adults (Herpertz-Dahlmann, Seitz, & Konrad, 2011). Therefore, understanding the neuropsychological profile of AN specifically in adolescence is crucial as this is the period in which AN typically has its onset. As a result, adolescents are less likely to have a long duration of illness and malnutrition. Thus, a greater understanding of the adolescent neuropsychological profile will aid in unravelling this complex picture.

Given that adolescents and adults may display different patterns of strengths and weaknesses due to differences in developmental stages, and likely differences in duration of illness, which may affect their functioning, applying the adult literature base

to younger populations is not always appropriate (Kerem & Katzman, 2003). There have been recent systematic reviews published in the literature about the current evidence base in younger populations with AN with regard to central coherence (Tchanturia & Lang, 2014) and set-shifting ability (Lang, Stahl, Espie, Treasure, & Tchanturia, 2014), aspects of executive functioning. However, there have not been any recent reviews that have specifically examined the neuropsychological research base as a whole in this population. For increasingly time-poor and highly pressured clinicians working in this field, it is beneficial to have a review of the current literature that encompasses the broad profile as opposed to only considering discrete cognitive domains. This will enable clinicians to design and conduct appropriate neuropsychological assessments for individuals in their care.

Aims

Therefore, the aims of this study are to critically review the available peer-reviewed literature concerning the neuropsychology of adolescents with AN, including cohort and case-control studies. The purpose of this review is to help inform clinicians working with this young population about the current state of the evidence base of what is known about the broad neuropsychological profile of AN during this developmental period.

Providing a critical synthesis of the evidence base using a systematic methodology has a two-fold objective. Firstly, we hope that this will be an aid to practitioners working with this population when considering what neuropsychological assessments may be warranted clinically and what tools are often used. It is also hoped that it will it indicate current gaps in knowledge which could be filled by pursuing practice-based evidence in specialist teams that have access to these rare populations.

One of the difficulties in doing this research in AN, is the lack of access to large data sets in order to have sufficiently powered studies.

The research questions are:

- Do adolescents with anorexia demonstrate any specific pattern of strengths and/or weaknesses across their neuropsychological profile?
- Are there differences in adolescents when tested in underweight versus weight-restored states?
- If patterns are observed, are these similar to or distinct from those observed in adults with AN?

Methodology

This systematic review was carried out according to the PRISMA statement (preferred reporting items for systematic review and meta-analysis) (Moher, Liberati, Tetzlaff, & Altman, 2009). Please see Figure 1 that depicts the consort diagram for the study selection.

Inclusion and Exclusion Criteria

Study inclusion and exclusion criteria are listed below. Given that adolescents are often seen in Child and Adolescent Mental Health services in the UK up to 19 years of age, it was decided that including samples where the cohort mean age did not exceed this age range was appropriate. As studies do not always report age ranges, it was deemed acceptable to include studies whose upper age limit may be older than 19 years old, as long as it met the previously stated criterion and individuals appeared to have onset of AN within adolescent years. Focusing on those abilities most commonly

included in neuropsychological assessments seemed pertinent, given the intended audience of this review (i.e. clinical practitioners). Therefore, it was decided to focus on tasks that have been employed and standardised for clinical use, as opposed to purely experimental research. Some method of ranking neuropsychological functioning needed to be included, so studies must have utilised some comparison sample; either normative data or a control group. Given time and funding limitations, only those studies published in English were applicable, though this did not preclude studies that may have been conducted in non-English speaking countries. Similarly, this extended to the inclusion of grey literature (e.g. unpublished data from theses) as time constraints would have prevented a thorough search of this evidence.

It must be noted that no one neuropsychological task is a pure measure of the functioning of a specific cognitive domain, as all tasks will require various different systems to be functioning in tandem with each other in order to perform any given task (Steinglass & Glasofer, 2011). This means that a single task may be measuring functioning of multiple domains working simultaneously, and if impairments are noted in any one task, it may not be the result of a single dysfunctional cognitive domain. While it is recognized that separating tasks into specific cognitive domains is therefore somewhat artificial, we were guided by what each research group decided each task was measuring in their testing battery as a means of structuring our analyses.

Studies were **included** if:

1. Participants were human.
2. Participants were diagnosed with AN.
3. The mean age of the sample was 19 years or under (to distinguish it from mixed adult/adolescent samples).
4. Participants were assessed within an acute and/or weight-restored state.

5. Analyses for the adolescent age group were reported separately from adult populations (up to and including a mean age of 19 years old for separate groups).
6. They included at least one standardised neuropsychological outcome measure in their testing battery, as opposed to a purely experimental task.
7. Behavioural measures of neuropsychological performance were included, as opposed to self-report measure, e.g. studies only using the Behavior Rating Inventory of Executive Function (BRIEF) questionnaire as a measure of executive functioning were excluded.
8. They were published in English.

Studies were **excluded** if:

1. Only a self-report measure of cognitive/neuropsychological performance was used.
2. No control group was employed, or no standardised and normed psychological measure was used.
3. The sample included range of eating disorder diagnoses, (e.g. AN, bulimia nervosa (BN) and Binge Eating Disorders (BED)), where no breakdown of results specifically by diagnosis was reported.
4. Studies only had one clinical participant.
5. The research was not published in peer-reviewed journals.

Search strategy

Searches were conducted up until March 2016 in six multidisciplinary electronic databases: Web of Science (n = 707), Scopus (1960 – present; n = 384), Medline (1946 – present; n = 682), Science Direct (n = 30) and lastly Embase (1974- present) and PsychINFO (1806 - present) using Ovid (n = 2667). No date restrictions were applied to the search. Search terms were developed by looking at previously published relevant

reviews. Terms relating to AN, adolescents, and neuropsychological domains were combined using the Boolean operators AND and OR strategies. For further details, please see Table 1. Both keyword and subject heading searches were conducted. For example, when searching in Medline, MeSH terms were included. When possible within the database in use, searches were limited to the use of human participants and studies published in the English language. In addition, a hand search of studies listed in the author's personal reference manager was conducted. This led to the addition of two more relevant papers.

Table 1

List of search terms

Construct	**Search Terms**	**Boolean Operators**	**Combining constructs**
Anorexia nervosa	anorexia, "anorexia nervosa"	OR	
Adolescence	adolescent, children, youth, "young people"	OR	AND
Neuropsychology	neuropsychology, cognition, neurocognition, neurodevelopment, intelligence, attention, memory, language, visuospatial, executive function, perception, reasoning	OR	AND

Selection and Review Strategy

Once the searches were conducted, the titles of each retrieved article in the search were screened for suitability, and subsequently the reference lists of each

retrieved previously published, relevant systematic reviews and meta analyses. Studies that appeared to broadly fit the remit of the study inclusion and exclusion criteria based on their title were marked within each database/review. All the marked articles in each database were then uploaded into reference manager software, Endnote. References were then de-duplicated (duplications = 368). If the title of each study did not provide enough information to determine inclusion according to the selection criteria, then the abstract was reviewed. Common reasons for exclusion at this stage included a non-eating disorder sample (n = 1783), non-human sample (n = 882), sample of mixed eating disorder or eating disorder other than anorexia (e.g. bulimia nervosa, binge eating disorder; n = 759), an adult sample (n = 694), treatment trials (n = 366), book, opinion piece or non-empirical paper (n = 227), no measure of neuropsychological functioning (n = 174), and studies that investigated cognitions as opposed to cognitive/neuropsychological functioning (n = 89). For those that remained seemingly eligible, full text articles were retrieved (n = 130).

Where full-text publications of potentially relevant research were unavailable through University College London subscriptions to journals, authors of these studies were contacted directly through Research Gate and subsequently full-text copies were made available. Reasons for exclusion at this stage included the age range being too wide or no separate reporting of results for adolescent participants (n = 52), no standardized, direct measure of neuropsychological functioning (n = 9), full-text publications unavailable in English (n = 6), gray literature (e.g. theses; n = 5), review articles (n = 5), conference proceedings (n = 5), mixed eating disorder samples with no separate reporting for AN group (n = 4), assessments not typically carried out in clinical/mental health settings (e.g. haptic perception; n = 3), case studies (n = 2) or assessment of cognitions (i.e. thoughts), not cognition (n = 3). Following this, 36 articles were deemed eligible for inclusion in the sample. In the studies under review,

both cohort studies and case series were included as both were considered to aid the overall understanding of this context. Finally, the reference lists of these included papers were reviewed, but no more non-duplicate relevant studies were found.

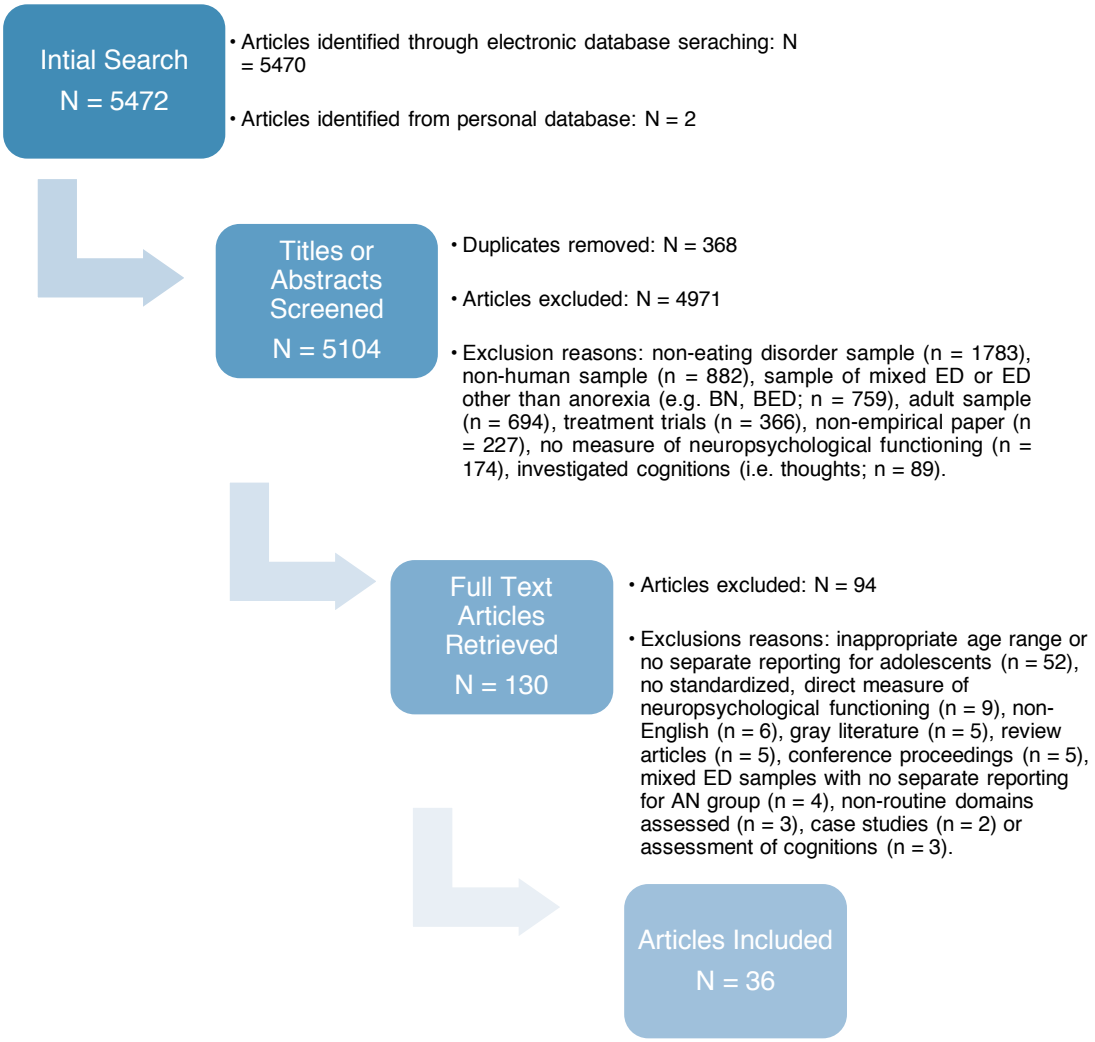

Figure 1 - Flow diagram of selection process

Extraction

A standardised form was developed prior to the data extraction process detailing the study characteristics, study results and information required for the quality/bias assessment to be conducted. The author, who had no prior affiliation with any of the research groups and/or studies under review, extracted all the data independently. The

authors, date of publication, sample size, mean and standard deviation (SD) of age, age range, gender, mean and SD of age at onset, mean and SD of duration of AN, mean and SD of BMI, state of AN group at time of testing, presence of co-morbidities, presence of psychoactive medication, IQ level, cognitive domains assessed, neuropsychological tests used, overall findings, follow-up findings and criteria needed for the quality rating were all extracted and combined into a table (see Table 2 and Appendix I). Descriptive statistics, including means, standard deviations (SD) and sample size were extracted for each outcome measure included in the test battery to determine overall context and significance of findings. Significance levels and effect sizes (if reported) were also extracted with regard to any testing that investigated differences in group means on outcome measures. Given the number of outcome measures and domains of functioning under review, it was beyond the scope of this current review to conduct meta-analyses so a narrative synthesis will be presented.

Data will be presented: (i) comparing AN group performance to normative data, (ii) comparing AN and a control group for performance on measures and (iii) examining within-group differences during underweight and weight-restored states for AN groups in each cognitive domain in turn.

Quality Assessment

There are no currently available standardised criteria for assessing the quality of neuropsychological studies (Wu, Hartmann, Skunde, Herzog, & Friederich, 2013). Therefore, criteria were developed to assess the quality and risk of bias in these studies based on those set out in the Newcastle Ottawa Scale for non-randomised controlled trials developed by Wells and colleagues (2000). Based on a similar strategy used by two recent reviews (Wu et al., 2013;Reville, O'Connor, & Frampton, 2016), a set of

criteria were developed that took into account the selection of participants, the comparability of participants and how performances were established.

Studies as a whole were assessed according to the following criteria as to whether they were present or absent:

1) Included the exclusion criteria for participants in their reports
2) Gave an account of the diagnostic process and tools that were used
3) Whether a healthy control group was included in the sample
4) Whether case-control pairings were included in the sample
5) Whether a standardised outcome measure was used
6) Whether researchers controlled for co-variates in their research design or analysis
7) Whether there was an objective report of the dependent measure

This quality rating was carried out by the author. Each study was rated on each of the above criteria, and these were then totaled to give an overall score. Studies that were scored, 6-7 points were rated as 'high', 4-5 as 'medium' and 1-3 as 'low'.

Results

Study and Sample Characteristics

A summary of all the studies' characteristics can be found in Table 2. For the sake of readability throughout this section, all references to the studies under review will utilise their assigned study ID number, which can be found in this table. Publication dates ranged from 1981 to 2016; with the majority of studies being published since 2009 (n = 30). AN participants were diagnosed according to a range of widely accepted diagnostic

criteria including: numerous editions of the Diagnostic and Statistical Manual of Mental Disorders: DSM-R, DSM III-R, DSM IV, DSM-IV-TR, DSM 5, the International Classification of Diseases, 10th Edition (ICD-10; World Health Organization, 2004) and the Great Ormond Street Hospital diagnostic criteria for AN in childhood (Nicholls, Chater, & Lask, 2000).

Determining which criteria were to be used in each study appeared dependent on the date of recruitment to the study and age of the sample.

It was notable that most studies included a female only sample, (n = 30), with only a small number including a mixed gender sample (n = 5) and only one including a male-only sample (3). It was unclear in those studies that only included females whether being male was part of the exclusion criteria, or due to the unavailability of male participants. There is a known gender imbalance in prevalence rates in AN, especially in clinical samples (Sweeting et al., 2015). With regard to the age range of the samples under review, then youngest aged participants were 9 years old (15, 23), while the oldest were 27 years old (7, 23), with the narrowest age range between oldest and youngest participants being 3 years (8) and the widest age range being 18 years (23). Although, the modal age range was much narrower at 6 years (n = 8: 2, 13, 18, 19, 26, 29, 30, 33). This demonstrates the breadth of development stages under review, even when a strict age criterion is applied. This may limit the conclusions that can be drawn, given the continuing cognitive development that is taking place, underpinned by structural brain changes during this wide age period. The lowest mean Body Mass Index (BMI) score was 13.48 (15), while the highest was 17.02 (9), which again indicates the wide range in degree to which samples were underweight. Regarding duration of AN (noting the different criteria in measuring this variable), the shortest duration was 2.20 months (25) and the longest 32.9 months (13). Most studies tested

participants during treatment; however, the type of treatment and reporting of detail regarding the aim and content of this treatment varied widely.

Methodologies

Numerous methodologies were employed by the studies under review in order to test their hypotheses about neuropsychological functioning in adolescents with AN, using both cohort-studies and case series, cross-sectional and longitudinal designs. Commonly, studies used a healthy control group that was comparable in terms of gender, age and sometimes IQ level to compare against, while less frequently other studies compared performance to normative data (n = 8: 3, 6, 8, 9, 16, 21, 23, 34). However, four of these studies were case series (3, 6, 9, 21). Their specific aims were to compare individual neuropsychological profiles to each other on the same measures using the Ravello Profile, in order to investigate the individual variability in neuropsychological functioning within adolescents with AN. Another study tested their AN and HC groups using a comprehensive neuropsychological testing battery, dividing individuals in each group into "impaired" vs "normal" performers depending on whether their performance on two or more tasks fell below two standard deviations (SD) from the normative mean or their estimated intelligence level (24). There were also a number of studies that used a psychiatric control group in their sample (1, 32 35, 36), and one study that used a medical control group (35). Some studies divided their analyses in AN groups by subtype or used only one subtype (15); however, given the purpose of this review, the AN data will be analysed as a whole.

Treatment of Confounding Variables

There are multiple confounding variables that can influence neuropsychological test performance in individuals with AN including: state of starvation at testing,

duration of illness, use of psychoactive medication and co-morbid diagnoses (Jauregui-Lobera, 2013). The level of detail reported and method of handling these potential confounds varied widely within the studies under review. Some included those with any psychiatric co-morbidity, many only excluded those with more severe co-morbid diagnoses, such as bipolar disorder, schizophrenia (e.g. 14) and some chose to exclude any psychiatric co-morbidities from their clinical samples (e.g. 11), despite the common co-occurrence of mood, affective and obsessional disorders with AN. Several studies did not include this information in their reports (e.g. 2). Commonly, anxiety, depressive and obsessional symptoms were examined using a variety of standardised child and adolescent questionnaires and semi-structured interviews, such as the State Trait Anxiety Inventory (Spielberger, Goursuch, & Lushene, 1983), Children's Depression Inventory (Kovacs, 1984) and the Leyton Obsessional Inventory-Child Version (Berg, Rapoport, & Flament, 1986). Some studies chose to include patients who were currently taking commonly prescribed psychoactive medications in these populations, such as selective serotonin re-uptake inhibitors and atypical antipsychotics (e.g. 15), while others excluded them (e.g. 25, 26), and again, some did not report any such information (e.g. 23). In addition, some researchers used some of these variables as covariates in their analyses to understand their relative influence on the outcome measures (e.g. 15, 16). However, for the most part it was difficult to ascertain the relative influence these confounds may have had on outcomes due to the numerous methodological differences between these studies under review.

Quality Rating

In total, fifteen of the studies were ranked as "high" quality, meaning they were awarded a score of 6-7 on the quality scale. Eighteen studies were ranked as "medium" quality (scores of 3 to 5), while three studies were rated as being of "low" quality

(scores of 1 to 2). Please see Appendix I for further details regarding how each study was ranked.

Study ID	Author (Date)	Ss	Mean (SD) Age in Yrs	Age Range	Sex	Mean (SD) Age at Onset of AN	Mean (SD) AN Duration	Mean (SD) BMI (at baseline ax)	AN Testing State	Co-morbidities	Psychoactive Medication	IQ	Cognitive domains	Tests	Findings (Baseline)	Follow-up Findings
1	**Sarrar et al. (2016)**	AN: 47 PC: 21 HC: 48	AN: 16.2 (1.6) PC: 15.5 (1.4) HC: 16.4 (1.3)	NR	F	NR	NR	AN: 14.9 (1.30) PC: 22.52 (5.32) HC: 20.93 (2.47)	I/Ps and O/PS	Excluded if met criteria for diagnosis other than for particular group	AN not on medication, but 28.6% PC were	Culture Fair Intelligence Test: AN: 100.8 (8.75) PC: 104.4 (14.79) HC: 102.4 (10.47)	Intelligence Processing speed Executive Function: Cognitive Flexibility	probabilistic Object Reversal task (pORT), Card Sorting Test (version of WCST), Trail Making Tests a, Wechsler Intelligence Scales: Digit Symbol (DS)	1. AN performed worse than HC on Digit Symbol test ($p = 0.06$, $n2 = 0.051$) 2. Being in AN group resulted in higher chance of being in lower quartile of performance on DS compared to HC ($p< 0.05$), TMT and pORT ($p<0.10$)	N/A
2	**van Noort et al. (2016)**	AN: 20 HC: 20	AN: 15.6 (1.2) HC: 15.7 (1.1)	12-18 yrs	F	NR	NR	AN: 15.7 (1.4) HC: 21.7 (2.2)	1. I/Ps and O/PS in treatment 2. Following 10 sessions of CRT	Anxiety and Depressive Symptoms assessed	NR	*Unknown test battery:* AN: 106.2 (14.7) HC: 110.1 (11.7)	Executive Function	Delis-Kaplan Executive Function Scales (D-KEFS): TMT 4, Rey-Osterrieth Complex Figure Test (RCFT)	1. NS group differences on any measure	1. Relative to baseline, AN performed better at follow-up on TMT 4 ($p= 0.004$), central coherence on RCFT ($p= 0.014$), whereas the HC only performed better on central coherence on RCFT (p=

															0.003) but not TMT 4 (p= 0.720)
3	**Stedal & Dahlgren (2016)**	AN: 10	AN: 15.7	14-18 yrs	M	NR	NR	AN: 4.5%ile (8.5)	During weight restoration treatment	Anxiety, depressive and obsessional symptoms were assessed	NR	Wechsler Abbreviated Scales of Intelligence (WASI; Vocabulary & Matrix Reasoning): AN: 107.3 (9.82)	Intelligence Executive function, Central coherence, Visuospatial memory, Verbal fluency	WASI, D-KEFS): TMT 4 Colour word interference test (CWI) 3 and 4 Tower test (Tower) The Brixton Test Brixton spatial anticipation task RCFT	1. AN group as a whole scored within average range on all measures 2. Wide variability in individual profiles, with less divergence in executive functioning tasks (D:KEFS tasks: z scores from 0.5 to -1.3), and greater divergence in visual spatial (z scores from 1.1 to -2.5) and verbal fluency tasks (z scores from 2.8 to -2.2)	N/A

4	**Kjaersdam Telléus et al. (2015)**	AN: 94 HC: 94	AN: 14.9 (1.8)	10-17 yrs	F (89.4%) and M	NR	1.2 (1.2) yrs	AN: 15.8 (1.8)	I/Ps and O/PS	Screened for psychiatric co-morbidities and autism		Wechsler Adult Intelligence Scale 3rd Ed. (WAIS III)/ Wechsler Intelligence Scale for Children 3rd Ed. (WISC III): FSIQ AN: 101.1 (16) HC: 102 (13.4)	Intelligence Executive Functioning Working Memory Attention Processing Speed Visual Memory Spatial Memory Verbal Memory	WISC III/WAIS III, (all core subtests), RCFT, TMT a&b, Cambridge Neuropsychological Test Automated Battery (CANTAB): Stockings of Cambridge, IED, Spatial Span, Spatial Working Memory, rapid visual information processing, simple and choice reaction time (RTI), pattern recognition memory, spatial recognition memory, Tests of Learning and Memory (TOMAL 2): Memory for stories (immediate and delayed), Word selective reminding (immediate and delayed)	1. AN group scored worse than HC on perceptual organisation index (POI) of WISC III/WAIS, ($p= 0.009$), 2. No sig. group differences on any other IQ index 3. Greater discrepancy between VCI and POI in AN vs HC ($p= 0.001$) and between VIQ and PIQ ($p=0.006$) 4. AN group were slower than HC on some motor speed tasks (RTI subtests: $p< 0.05$) 5. AN performed more poorly than HC on short term verbal memory (memory for stories: $p= 0.009$) 6. AN group performed better an HC on visuoconstruction task (RCFT copy: $p= 0.003$) 7. NS groups differences on all measures of set shifting or any other measure	N/A

5	**Lang et al. (2015)**	AN: 41 HC: 43	AN: 15.0 (1.8) HC: 15.1 (1.9)	11-18 yrs	F	NR	1.7 (1.18) yrs	AN: 16.16 (1.50) HC: 20.34 (1.99)	I/Ps and O/PS in treatment	Anxiety, depressive and obsessional symptom assessed, autism screened	Yes - Described in detail in sample	WASI: FSIQ AN: 105.9 +/- 21.30 HC: 105.3 +/- 11.81	Intelligence Executive Functioning: Set Shifting Central Coherence	WASI (all 4 subtests), Wisconsin Card Sorting Task (WCST), RCFT, Fragmented Pictures Task (FPT)	1. No group differences between AN and HC on any IQ scales/sub-scales 2. AN displayed no impairments on any measures relative to norms 3. On WCST, AN showed set-shifting impairments relative to HC ($p < 0.01$) 4. On RCFT, AN showed impairments relative to HC ($p < 0.01$)	N/A
6	**Stedal & Dahlgren (2015)**	AN: 20	AN: 15.9 (1.6)	13-18 yrs	F	NR	NR	AN: 10.2%ile (17.2)	I/Ps and O/PS in treatment	NR	NR	WAIS/WASI: VIQ: Vocabulary/PIQ: Matrix Reasoning: reported as in normal range	Intelligence Executive Functioning: Cognitive Inhibition, Verbal Fluency, Switching, Planning & Inhibition, Flexibility & Spatial Working, Memory: Visuo-spatial Memory, Visual Spatial Processing	WAIS III/WASI: Matrix Reasoning, Vocabulary; Ravello Profile: D-KEFS (Colour Word Interference (3&4) Verbal Fluency (1, 2, 3) Trail Making Test (4) Tower of London), Brixton Spatial Anticipation Test, RCFT	1. Scores on all measures fell within the normal range	N/A

7	**Overas et al. (2015)**	AN: 30 HC: 45	AN: 19.0 (2.9) HC: 18.3 (3.1)	14-27 yrs	F	NR	NR	W/H Ratio AN: 77.53 (7.48) HC: 101.29 (13.00)	In treatment	Anxiety and Depressive Symptoms assessed	NR	WAIS III/WISC III - Matrix Reasoning - AN:11.0 (2.83), HC: 11.8 (2.01) Vocabulary: AN: 10.31 (1.82) HC: 10.39 (2.31)	Intelligence Executive Function: Set Shifting	WAIS III/WASI: Matrix Reasoning, Vocabulary; WCST	1. AN group performed worse on several indicators of WCST ($p < 0.05$), however scores for both AN and HC still lay within 1SD of normative mean 2. W/H was positively correlated with both non-perseverative errors ($p< 0.01$) and conceptual level responses ($p < 0.05$).	N/A
8	**Breithaupt, Payne, & Rose (2014)**	AN: 9	AN: 16 +/- 1	14-17 yrs	F	NR	NR	AN: 13.89 (1.77)	I/Ps during first two mths of admission	Obsessional symptoms assessed	NR	WASI: AN: Matrix 0.09z (1.13) Vocab - 0.22z (0.66)	Intelligence Executive Functioning: Cognitive Inhibition, Verbal Inhibition, Verbal Fluency, Switching, Planning, Flexibility, Inhibition, Set Shifting	Aspects of Ravello Profile: D-KEFS-Colour Word Interference (3&4) Verbal Fluency (1, 2, 3) Trail Making Test (4) Brixton Spatial Anticipation Test, Hayling Test	1. IQ subtests fell within average range for all AN sample	N/A
9	**Dahlgren et al. (2014)**	AN: 20	AN: 15.9 (1.7)	13-18 yrs	F	NR	2.4 (1.9) yrs	AN: 17.02 (1.67)	I/Ps and O/PS in treatment	Anxiety, depressive assessed	NR	WAIS III AN: PIQ 11.5 (3.0), VIQ: 10.4 (0.9) /WASI: AN: PIQ: 56.3 (6.6)/WISC-III VIQ: 9.2 (3.2)	Intelligence	Vocabulary Matrix Reasoning	1. AN group had VIQ and PIQ mean scores that fell within the average range	N/A

10	**Fornasari et al. (2014)**	AN: 15 HC: 15	AN: 15.4 (1.2) HC: 15.4 (1.1)	13-17 yrs	F	14.00 (1.31)	13 mths (median)	AN: 17.02 (1.11) HC: 20.64 (1.99)	Unknown	Described psychiatric co-morbidities present: OCD (n=1), Mood disorders (n=2)	Yes - 1 AN on SSRI	Raven Standard Progressive Matrices: AN: 98th %ile, HC: 94th%ile	Intelligence Executive Functioning	Computerised Iowa Gambling Task (IGT), Computerised N-back	1. AN group was impaired on aspects of IGT compared to HC (p= 0.028) 2. NS differences between AN and HC groups on n-back task	N/A
11	**Lozano-Serra et al. (2014)**	AN: 25 HC: 26	AN: 15.1 (1.2) HC: 15.5 (1.6)	11-18 yrs	F	NR	12.26 (8.1) mths	AN: 15.4 (1.6) HC: NR	1. During I/P/day patient treatment 2: After 6 mths of MDT treatment	Psychiatric co-morbidities excluded from sample, Anxiety, depressive and obsessional symptoms assessed	NR	WISC-R: Vocabulary used as IQ estimate: AN: 10.6 (2.6) HC: 11.2 (2.0)	Intelligence Memory: Visual Immediate and Delayed Recall Executive Functioning Attention	WISC-R: Vocabulary and Block Design, Wechsler Memory Scales III (WMS III): Visual Reproduction, RCFT, TMT a&b, WCST, Stroop Test	1. AN group performed worse than HC group on aspects of RCFT (immediate recall, time to copy & organisation, p< 0.05) 2. NS groups differences on all other measures	1. Relative to baseline, both AN and HC groups' performance improved (p= 0.026), no further specific details reported
12	**Rose et al. (2014)**	AN: 78 HC: 78	AN: 15.2 (1.8) HC: 15.2 (1.8)	10-18 yrs	F	NR	NR	AN: 15.9 HC: 21.1	NR	Anxiety, depressive and obsessional symptoms assessed	NR	WASI (2 IQ) Vocabulary & Matrix Reasoning) : AN: 108 (10.9) HC: 104 (10.9)	Intelligence Visuospatial Memory Central Coherence	WASI: Vocabulary & Matrix Reasoning, RCFT	1. AN group took longer to copy the RCFT and scored higher on accuracy than HC group (p < 0.01) 2. NS group differences on immediate, delayed, recognition memory, central coherence or organisational strategy scores on RCFT 3. AN group had higher FSIQ score than	N/A

														HC group (p = 0.046)	
13	**Wierenga et al. (2014)**	AN: 11 HC: 12	AN: 16.0 (2.0) HC: 14.9 (1.8)	12-18 yrs	F	NR	32.9 (24.1) mths	AN: 16.9 (1.5) HC: 20.8 (1.6)	Receiving family-based treatment and consuming 75-100% of daily calorie needs	Anxiety and Depressive Symptoms assessed, 39.1% AN met criteria for depression	N - Initially Ss later excluded from analyses	WASI: Matrix Reasoning - AN: 55.6 (4.0) HC: 56.6 (3.8) Similarities AN: 56.8 (9.2) HC: 57.9 (9.8)	Intelligence Academic Achievement Executive Function	WASI: Similarities and Matrix Reasoning, Wide Range Achievement Test Revision 4 (WRAT 4): Reading subtest, WCST	1. AN group performed worse than HC group on aspects of WCST, making more perseverate errors (p= 0.03) 2. NS group differences on all other measures, with AN groups scoring within average range	N/A
14	**Zwipp et al. (2013)**	AN: 72 rAN: 23 HC: 52	AN: 17.8 (3.4) rAN: 20.7 (3.8) HC: 17.7 (3.0)	NR	F	NR	NR	AN: 15.1 (1.3) AN-rec: 20.3 (1.4) HC: 21.7 (2.0)	During weight restoration treatment	Excluded AN Ss if met criteria for schizophrenia, substance dependence, bipolar, BN or BED	No: Excluded from sample	Not assessed	Psychomotor Speed Attention	TMT a	1. NS group differences between AN and HC on TMTa performance	N/A
15	**Calderoni et al. (2013)**	AN: 23 HC: 46	AN: 13.4 (2.0) HC: 23.4 (2.0)	9-16 yrs	F	12.18 (2.21) yrs	15.52 (11.86) mths	AN: 13.48 (2.04) HC: 13.48 (2.02)	I/Ps during treatment	Described psychiatric co-morbidities present in AN: OCD (n=1), Mood disorders (n=10)	Yes - Described in detail, 4 AN: atypical antipsychotics, 4 AN: SSRI	WISC-III (n= 17 AN): V IQ: 111.3 (14.44) PIQ: 108.4 (13)	Intelligence Attention Executive Functioning Language Memory and Learning: Verbal and Visuospatial Sensorimotor Functioning Visuospatial Processing *(Social Perception- not reported here)*	WISC-III, NEPSY-II: all 31 subtests	1. With regard to each cognitive domain index, NS group differences between AN and HC on each domain 2. AN performed worse than HC on response set (EF) task (p=0.033), 3. AN performed better than HC on semantic word generation task (p=0.029), which	N/A

															latter analyses revealed to be explained by presence of mood disorder	
16	**Dahlgren et al. (2013)**	AN: 20 (n=17 in neuropsychological ax)	AN: 15.9 (1.6)	13-18 years	Female	NR	2.7 (2.1) years	AN: 16.81 (1.63)	Inpatients and outpatients in MDT treatment aimed at weight restoration	Anxiety and Depressive Symptoms assessed	NR	Unknown test battery: All participants scored within normal range of VIQ and PIQ subtests at baseline	Visuospatial Memory, Visuospatial processing, Verbal Fluency, Executive Functioning	The Ravello Profile: RCFT, D-KEFS Verbal Fluency, TMT 4, Colour Word Interference 3&4, Tower of London, Brixton Spatial anticipation test; Group Embedded Figures Test (GEFT)	1. All baseline measures fell within normal range for AN group	1. Following CRT treatment, AN group performance improved on all measures, but only significantly relative to baseline on aspects of RCFT, GEFT and letter fluency ($p < 0.01$) 2. Weight increases influenced these significant

															improvements on RCFT and letter fluency, while improvement in depressive symptoms influenced GEFT task (p <0.05)
17	**Stedal et al. (2013)**	AN: 52 HC: 37	AN: 18.7 (3.1) HC: 17.6 (2.9)	13-25 yrs	F	NR	NR	AN: 16.8 (2.0) HC: 21.6 (2.9)	NR	No exclusion of patients with co-morbidities	No exclusion of patients taking medication, but no description of Ss reported	N/A	Language Verbal Fluency	WAIS-III: Vocabulary, D-KEFS: Verbal Fluency	NS group differences between AN and HC on Vocabulary (p = 0.885)	N/A
18	**Buhren et al. (2012)**	AN: 28 HC: 27	AN: 15.6 (1.5) HC: 15.0 (1.7)	12-18 yrs	F	NR	11.2 (7.4) mths	15.4 (1.2)	1. I/Ps and O/PS in treatment 2. At discharge for follow-up	Described psychiatric co-morbidities present in AN: Depression (n=20), Excluded AN Ss if met criteria for schizophrenia, substance dependence, bipolar, BN or BED	1. No, at baseline 2. At follow-up, AN: 5 atypical antipsychotics, 2 AN: SSRI	WISC (tested at follow-up): FSIQ: AN: 108.8 (10.4) HC: 109.3 (14.2)	Intelligence Executive Functioning: Set-Shifting	Amsterdam Neuropsychological Tasks Program: Visual Set Shifting Task	1. Relative to HC, AN group had slower reaction times (p <0.05) but made fewer errors (p <0.05) on set-shifting task 2. Relative to HC, AN group had longer RTs on shift vs non-shift trials at baseline (p< 0.001)	1. Relative to HC, AN group had slower reaction times (p <0.05) but made fewer errors (p <0.05) on set shifting task 2. 2. Relative to HC, AN group had longer

															RTs on shift vs non-shift trials at follow-up (p< 0.001)
19	**Fitzpatrick et al. (2012)**	AN: 32 HC: 22	AN: 14.9 (1.8) HC: 15.4 (1.8)	12-18 yrs	F	NR	NR	Not reported but Median Body Weight-AN: 78.04% (6.55) HC: 105.69 % (1.89)	NR	AN excluded from sample if had psychosis, BED or EDNOS	NR	WAIS III/WISC IV (4 core subtest version-prorated)-AN:119.5 (14.50), HC: 119.5 (11.95)	Intelligence Executive Functioning: Set Shifting	Computerised WCST 4, D-KEFS (TMT, Verbal Fluency, Colour Word Interference), Brixton Spatial Anticipation Task	1. No group differences in IQ 2. No group differences on any measure of set-shifting ability 3. AN group had slower motor speed (p = 0.008)	N/A
20	**Frampton et al. (2012)**	AN: 15 HC: 15	AN: 19.0 (1.9) HC: 18.3 (2.2)	14-21 yrs	F	Early Onset (Before 14 yrs)	NR	W/H Ratio AN: 88.13 (10.15) HC: 106.39 (13.80)	12/15 recovered, 1 AN & 2 now BN	NR	NR	Matched FSIQ using WASI: AN 113.2 (12.19) HC: 114.2 (9.79)	Intelligence Executive Function Visuospatial Memory Visual Perception	D-KEFS (Tower Test, TMT, Verbal Fluency, Colour-Word Interference), RCFTs Hayling Sentence Completion Test, Silhouettes	1. NS overall between group differences on any measure 2. Differences between hypo perfused and normally perfused AN subgroups and HC groups on delayed visual recall (p< 0.001)and verbal inhibition (p< 0.05)	N/A

21	**Rose et al. (2012)**	AN: 9	AN: 14.7	12-16 yrs	F	NR	NR	AN: 16.13 (1.35)	Unknown	Assessed for presence of anxiety, mood & depressive symptoms	NR	WASI AN: FSIQ: 103.67 (10.31) Vocab: 53.22t (8.21) Matrix Reasoning 51.44t (5.46)	Intelligence Visual Memory Central Coherence Executive Functioning	The Ravello Profile: DKEFS (TMT, Verbal Fluency, Colour Word Interference, Tower), RCFT Hayling and Brixton Test	Broad spectrum of neuropsychological strengths and weaknesses when looking at individual AN profiles, with wide variability	
22	**Shott et al. (2012)**	AN: 15 HC: 16	AN: 14.8 (1.1) HC: 14.0 (1.6) AdAN: 26.2 (7.2) AdHC: 26.0 (5.3)	NR	F	AN: 13.6 (2.1) yrs AdAN: 16.8 (0.4)	AN: 0.9 (0.8) AdAN: 9.1 (8.4) yrs	AN: 16.2 (1.1) HC: 20.5 (2.2) AdAN: 16.4 (1.3) AdHC: 21.8 (1.8)	I/Ps, day patients and O/PS in treatment	Yes - Screened for psychiatric co-morbidities : 5 AN & 14 AdAN: depression, 8 AN & 12 AdAN: anxiety disorders, No Ss had psychotic, substance use or bipolar disorders	Yes - 13 AN & 20 AdAN psychoactive medication (SSRI & atypical antipsychotic)	N/A	Executive Functioning: Set-shifting	Novel Category Learning Task	1. NS group differences in set-shifting performance on task	N/A
23	**Stedal et al., (2012)**	AN: 155	AN: 17.1 (3.2)	9-27 yrs	F and M	NR	NR	AN: 16.3 (2.0)	I/Ps and O/PS in weight restoration treatment	NR	NR	WASI/WAIS III: AN VIQ (Vocab): 107.7; PIQ (Matrix Reasoning) : 103.3	Intelligence Visual Memory, Central Coherence Executive Functioning	The Ravello Profile: RCFT, D-KEFS Verbal Fluency, TMT 4, Colour Word Interference 3&4, Tower of London, Brixton Spatial Anticipation Test	1. AN scored better than normative mean on verbal and non-verbal reasoning task ($p<0.05$) and verbal fluency tasks ($p<0.001$) 2. AN scored worse on all visuospatial tasks and central coherence	N/A

															measure (p< 0.01)	
24	**Andres-Perpina et al., (2011)**	AN: 37 HC: 41	AN: 15.4 (1.5) HC: 15.4 (1.5)	11-18 yrs	F and M	13.2 (1.7) yrs	13.9 (2.7) mths	AN: 15.3 (1.4) HC: not reported	I/Ps and O/PS in acute phase of disorder	Excluded if met diagnostic criteria for any other psychiatric disorder; anxiety, depression and obsessional symptoms reported	Yes, 8 AN: SSRI	WISC-R: Vocab used as IQ estimate but not reported	Intelligence Memory: Visual memory and perception, Verbal memory Executive Functioning Language: Verbal Fluency	Wechsler Memory Scale III, RCFT, Rey Auditory Verbal Learning Test (RAVLT), TMT, WCST, Controlled Oral Word Association Test, Stroop Test	1. Difference between AN and HC on visuoconstruction processing speed task (Time to Copy in RCFT) 2. AN (30%) deemed to show more impaired cognitive profiles relative to their IQ level, than HC (7%) (p = 0.01)	N/A
25	**Dmitrzak-Węglarz et al. (2011)**	AN: 61 HC: 49	AN: 15.85 (2.1) HC: 15.32 (2.1)	NR	F	13.48 (2.16) yrs	2.20 (1.79) mths	AN: 14.35 (1.55) HC: 20.54 (1.95)	I/Ps in acute phase of disorder during initial week of admission	Excluded Ss with schizophrenia and bipolar disorders	No, exclusion of Ss taking medication	Not assessed	Executive Functioning	WCST	1. N.S. group differences on WCST performance	N/A
26	**McAnarney et al. (2011)**	AN: 24 HC: 37	AN: 16.3 (1.2) HC: 15.9 (1.5)	14-20 yrs	F	NR	NR	AN: 16.7 (1.3) HC: 22.3 (3.7)	NR	Excluded if met criteria for psychiatric /developmental co-morbidities	No, exclusion of Ss taking medication	Kaufman Brief Intelligence Test-2 (KBIT2): AN: 111.6 (10.7),	Intelligence Executive Functioning	WCST, CANTAB: Intra/Extradimensional Shift (IED)	1. AN group made fewer errors on WCST (p = 0.011) 2. No group differences in performance on IED	N/A

									, screened for depression and OCD		HC: 113.1 (10.2)					
27	**Nagamitsu et al. (2011)**	AN: 16 HC: 12	AN: 14.2 (1.3) HC: 14.3 (1.3)	NR	F	14.2 (2.7) yrs	NR	AN: 16.2 (2.8) HC: 18.7 (1.3)	Post weight restoration and treatment	No anxiety, mood, psychiatric or developmental disorders present	NR	Not assessed	Language: Verbal Fluency	Word Fluency Task	1. NS group differences in number of words generated	N/A
28	**Sarrar et al. (2011)**	AN: 30 HC: 28	AN: 16.2 (1.2) HC: 16.3 (1.3)	14-18 yrs	F	NR	NR	AN: 15.0 (1.2) HC: 20.5 (2.5)	1. After admission for treatment 2. After weight gain	Co-morbidities present in sample described: 5 AN: affective disorder, 2 AN: OCD	NR	Culture Fair Intelligence Test (CFIT-20 R): AN: 100.7 (9.1), HC: 101.1 (9.2)	Intelligence Executive Function	probabilistic Object Reversal task (pORT), TMT a, Wechsler Intelligence Scales: Digit Symbol (DS)	1. NS group differences in TMT or DS at baseline 2. AN displayed poorer performance than HC on pORT ($p< 0.05$)	1. After weight gain, AN still displayed poorer aspects of performance on pORT than HC ($p= 0.024$), but improved relative to previous performance on TMT ($p< 0.001$) and many pORT variables ($p< 0.05$), and IQ ($p= 0.011$)

29	**Hatch et al., (2010)**	AN: 37 HC: 45	AN: 15.16 (1.6) HC: NR	12-18 yrs	F	NR	9.74 (10.11) mths	AN: 16.10 (0.93) HC: normal range for age	1. Within 3-10 days of admission for I/P treatment 2. Following weight gain	Assessed for presence of anxiety and mood symptoms	NR	Pre-morbid IQ estimate: 'Spot the Word' Test: AN: 43.6 (5.05), HC: 42.5 (5.12)	Attention, Timed Information Processing, Sensori-motor function, Executive Functioning	IntegNeuro battery: Verbal Interference, Switching of attention, choice reaction time, verbal learning & recall, digit span, span of visual memory, sustained attention, tapping, letter fluency and semantic fluency, Maze, Time estimation, Go no-Go, Auditory Oddball	1. Relative to HC group, AN group performed more poorly on Tapping, Choice Reaction Time, Go no-Go tasks and Verbal Recall ($p < 0.01$), but performed better on Digit Span reverse task ($p = 0.01$)	1. After weight gain relative to HC, AN performed better on aspects of Switching of Attention Task, Letter Fluency, reverse Digit Span, Maze, Verbal Interference and Sustained Attention tasks, but worse on the memory recognition task ($p < 0.01$). 2. Relative to baseline while underweight, AN performed better on aspects of tapping, switching of attention, verbal

																interference and memory recall tasks (p< 0.01) but worse on memory recognition task (p = 0.001)
30	**Castro Fornieles et al. (2009)**	AN: 12 HC: 9	AN: 14.5 (1.5) HC: 14.6 (3.2)	11-17 yrs	F and M	NR	8.3 (3.1) mths	AN: 14.8 (2.0)	1. I/Ps at admission 2. Following weight gain	No co-morbid psychiatric or medical conditions were present in sample, anxiety and obsessional symptoms were examined	NR	WISC-R: Vocab used as IQ estimate- AN: 46.8 (5.9) HC: 48.8 (5.2)	Intelligence Attention, Visual Processing, Visual Memory, Visuospatial ability	WISC-R: DS, Coding, Block Design, Similarities, RCFT	1. NS group differences between AN and HC on all measures, aside from Digit Span where AN performed more poorly (p= 0.046)	1. NS group differences between AN and HC at follow-up on all measures

31	**Neumarker et al. (2000)**	AN: 18 HC: 25	AN: 14.5 (1.5) HC: 15.8 (1.5)	NR	F	NR	267.83 (215.76) days	AN: 14.9 (1.36) HC: 20.5 (2.3)	1. I/Ps at admission 2. Following weight gain	NR	NR	CFT 20: Basic Intelligence test Scale 2 IQ12: AN (T1): 103.89 (10.07) AN (T2): 111.50 (11.60) HC: 111.64 (14.77)	Intelligence Language Arithmetic	CFT 20: Vocabulary battery and Number Sequence battery	1. AN performed poorer than HC on the Number sequencing test ($p < 0.05$) 2. NS group differences on basic intelligence or Vocabulary tests	1. After weight gain, there were no sig. group differences between AN and HC on any measure 2. Compared to baseline, AN group improved on basic intelligence test and number sequencing ($p < 0.01$)

32	**Blanz et al. (1997)**	AN: 160 BN: 30 PC: 95	AN & BN: 15.4 (1.9) HC: 15.4 (1.9)	NR	F and M	NR	NR	NR	During first two weeks of admission to outpatient and I/P treatment	NR	NR	Prufsystem fur Schul- und Bildungsberatung (PBS): FSIQ AN: 116.5 (13.9) BN: 114.0 (11.8) PC-AN: 104.4 (12.5) PC-BN: (102.9)	Intelligence Attention	All 9 subtests of PBS: Verbal, Non-verbal and Attention	1. AN & BN have highly FSIQ scores than PC control groups ($p< 0.001$) 2. AN & BN groups outperformed PC groups on verbal, non-verbal and attentional subtests ($p< 0.001$) 3. No group differences between AN & BN 4. No differences between verbal and non-verbal functioning within AN group, but BN group showed discrepancy with higher non-verbal vs verbal scores ($p< 0.05$)	N/A
33	**Bradley et al. (1997)**	AN: 20 HC: 20	AN: 15.7 (1.3) HC: 15.7 (1.2)	12-18 yrs	F	NR	NR	AN: 15.7 (1.2) HC: 21.2 (2.65)	1. I/Ps and O/PS in treatment 2. Following weight gain (@least 10% W/H)	Depressive symptomology was screened for	NR	Peabody IQ at T1: AN: 116.7 (14.86) HC: 113.4 (12.21); WISC-R at T2	Intelligence, Auditory Processing, Visual Processing, Memory: Verbal and Non-Verbal, Attention	Dichotic Words, Visual Dot Enumeration, Visual Search Test, Mental Rotation Task, Denman Neuropsychological Memory Test: Nonverbal & Verbal scales, Judgement of Line Orientation, Card Rotations Test, Perceptual Closure Test, WISC-R: Coding Fs, Digit-Symbol	1. NS group differences between AN and HC on all measures	1. Some improvement in both AN and HC groups on tasks from baseline to follow-up (no further details reported; n= AN: 8 HC: 8) 2. AN performed

													Paired Associates Learning Task, Continuous Performance Test		better than HC at follow-up on Card Rotations Test ($p < 0.05$) and Coding F's Task ($p< 0.05$)
34	**Dura & Bornstein (1989)**	AN: 20	AN: 14.7 (1.7)	12-17 yrs	F	NR	NR	NR	NR	NR	NR	WISC-R/WAIS-R: AN: 102.4 (11.84)	Intelligence Academic Achievement	All subtests of the WISC-R/WAIS-R and WRAT/WRAT-R	1. AN scored higher than predicted by VIQ and PIQ scores on Reading ($p < 0.05$) and Spelling Subtests ($p < 0.01$), but not on Arithmetic	N/A
35	**Witt et al., (1985)**	AN: 16 PC: 26 MC: 16 HC 16	AN: 16.4 (1.9) PC: 15.8 (1.2) MC: 16.1 (1.8) HC: 16.2 (2.0)	12-19 yrs	F	NR	NR	NR	During first two weeks of admission for I/P treatment	NR		WISC-R/WAIS-R: Pre-morbid IQ est. (Information): AN: 20.3 (3.1) PC: 10.3 (2.1) MC: 10.3 (2.4) HC: 11.2 (2.1)	Intelligence Visual Memory Learning Attention Psychomotor	WISC-R/WAIS-R: Information, Digit Span, Digit Symbol, WMS: Visual Reproductions, TMT b, Symbol-Digit Learning Test (SLDT)	1. AN group performed worse on multiple domains relative to PC, MC & HC groups on SLDT ($p <0.05$) 2. NS group differences between AN and CGs on all other measure.	N/A

36	**Wilbur & Collegian (1981)**	AN: 34 MC: 34 PC: 70	AN: 17 MC: NR PC: NR	10-22 yrs	F	16 yrs	12 mths	NR	During I/P treatment	Depressive symptomology self-reported	NR	WISC/WAIS (age-appropriate): FSIQ: AN: 111 vs PC: 99 ($p< 0.001$), VIQ: AN: 112 vs PC: 100 ($p< 0.001$), PIQ: AN: 109 vs PC: 99 ($p< 0.01$), NS differences between AN vs MC	Intelligence	WISC/WAIS	1. AN performed better on all IQ indices (FSIQ, VIQ and PIQ) than unmatched PC ($p < 0.01$).	N/A

Intelligence

While measuring intellectual functioning (IQ) in adolescents with AN has not been the main aim for most neuropsychological studies in the last two decades from looking at the publication dates of studies reviewed, most studies still included a measure of intellectual functioning as part of their testing battery (n = 31). Only five studies did not assess or report a measure or estimate of overall intellectual functioning (14, 17, 22, 25, 27).

A variety of tests (n = 9) were used either to measure or estimate the overall intellectual quotient (FSIQ) in their studies. Test batteries used included: Culture Fair Intelligence Test 1/2 (1, 28, 31), Wechsler Abbreviated Scales of Intelligence (WASI) (3, 5, 6, 8, 12, 13, 20, 23, 21), Wechsler Adult Intelligence Scales R/III (WAIS R/III)/Wechsler Intelligence Scale for Children R/III (WISC R/I) (4, 6, 7, 9, 11, 15, 18, 19, 23, 36), Raven Standard Progressive Matrices (10), Kaufman Brief Intelligence Test-2 (26), Spot the word test (29), Prufsystem fur Schul-und-Bildungsberatung (PBS; 32) and the Peabody IQ (33). There were two number of studies that did not report the name of the test used to measure IQ, but reported the range of scores (2, 16). Given the age range of these samples, often WAIS and WISC test batteries were used together, as the WISC is only for use with individuals up to 16 years 11 months. As might be expected in studies where IQ was not deemed as the main cognitive domain of functioning, often briefer measures such as the WASI were used to measure FSIQ, but the manner in which these test batteries were used was not uniform. Some used a two-subtest IQ estimate (e.g. 3, 8) but others used the four-subtest version (e.g. 5) of the WASI. While other studies used a single subtest score (e.g. Vocabulary subtest: 30, Information subtest: 35) or prorated from the four core subtests of the WISC/WAIS (19).

It must also be noted that in many of the studies reviewed, part of the study exclusion criteria was individuals with an IQ score of below 85 (>1SD from mean) or those that met criteria for a learning disability, which would mean by definition that their IQ score was below average. Therefore, it is unclear whether the presented scores above may be an over-estimate of general functioning within this group. These criteria were in place as often IQ functioning was not the main variable being investigated, and thus IQ was used as contextual information for understanding the other neuropsychological outcomes. For example, Andres-Perpina and colleagues (2011) found that there were more participants deemed as "cognitively impaired" in the AN group at 30% versus only 7% of the HC group. Their criteria for cognitive impairment required participants to have scored below 2SD or more from the mean on at least two tasks relative to their IQ or normative data (24).

In the majority of the studies reviewed where a measure/estimate of overall intellectual functioning was reported (n = 27), scores fell within the "*average*" range, defined as within one standard deviation of the normative mean for each test. However, it must be noted that their IQ scores most often fell in the upper half of the average range, which would put their group mean as being higher than the normative group mean. Less commonly, AN groups achieved a mean group score in what test batteries term the *"high average"* range (standard scores: 110-120; n = 8; 10, 15, 19, 20, 26, 31, 32, 33). In one such study, the AN group scored within the above average range, with the mean IQ score for the group falling at the 98th percentile using Raven's Standard Progressive Matrices (10). In another study, participants achieved a score that still fell within the high average range at 119.5, which was derived from a pro-rated four core subtest version of the WAIS III or WISC IV (19). It is interesting to note that despite clinical anecdotes that individuals with AN often appear to be highly intelligent, no

patient group displayed IQ scores that fell more than 1.5 SDs above the normative mean when measuring at group level in these 36 studies.

When mean IQ scores for the AN groups were compared to healthy control (HC) groups in studies where samples were not comprised of frequency-matched or case-control matched pairs on the basis of IQ (n = 13; 1, 4, 7, 11, 12, 13, 17, 18, 19, 28, 29, 30, 31), there was only one study that reported a statistically significant difference in mean FSIQ group scores using a two subtest version of the WASI (12). The authors of this study caution that this difference was of a small effect size, and only comprised of four IQ points. In another study that explored intellectual functioning much more comprehensively using the WAIS III/WISC III (4), widely considered to be the gold standard testing battery, they did find that AN displayed significantly lower scores than HC in the Perceptual Organisational Index (POI) score. More uneven profiles were also reported, with greater discrepancy between verbal (VIQ) and non-verbal (PIQ) reasoning indices and between verbal comprehension (VCI) and POI indices.

Interestingly, one study did not find any significant difference in intellectual functioning subtests (Vocabulary and Block Design) between acute AN and HC group at baseline (11). However, they also followed up their AN group after weight restoration, subdividing their AN group into those with amenorrhea and those who had experienced at least one menstrual cycle. They found that those continuing to experience amenorrhea performed significantly poorer on Block Design, an aspect of perceptual reasoning, than both menstruating AN individuals and HC group, despite there being no significant differences in BMI between the AN subgroups. It must be noted that the subgroup sample sizes were small, and hence, the study was likely to be underpowered.

Three studies used psychiatric control (PC) groups in their samples (1, 32, 26). The most recently published study found no difference between those with AN and

those with unipolar affective disorders using the Culture Fair Intelligence Test (1). However, the two much older studies found that the AN groups had significantly higher FSIQ scores than these mixed diagnoses PC groups (32, 36).

There were also differences in the timing of when IQ testing was completed across the studies. This is important to consider given the potential impact that being in a state of starvation at the time of the IQ testing may have (Duchesne et al., 2004). Of the three studies that tested aspects of intellectual functioning during both the acute and weight-recovered phases of AN (11, 28, 31), two found statistically significant improvements after weight-gain using the CFIT-20 (28) and the PBS (31). Some studies overcame the potential confound of starvation when testing individuals who were in an acute anorectic state by using a test that is thought to be a pre-morbid estimate of IQ, and therefore less sensitive to subsequent neurological impairment (e.g. Spot the Word Test: 29). It must be stated that this would only provide a crude estimate of intellectual functioning. Others that completed testing over two time points, only administered the full IQ testing battery once weight was restored (e.g. 33).

Processing Speed

Numerous tests were used in the studies (n = 10; 1, 4, 11, 14, 24, 28, 30, 33, 35) to measure aspects of processing speed including the Digit Symbol (1, 33, 35) subtest test from the Wechsler Scales, Coding F task (33), Trail Making Test Part A (TMT a; 1, 4, 11, 14, 28), Rey Complex Figure Test (RCFT; 11, 24, 30), Simple and Choice Reaction Time subtest from the CANTAB (4), and choice reaction time and tapping subtests from the IntegNeuro battery (29). While tests such as TMT and RCFT are often used as measures of a range of different cognitive skills, certain aspects of task performance on both have been identified as measuring aspects of processing speed;

namely part a of TMT with regard to time taken (Sanchez-Cubillo et al., 2009) and the time taken to copy the figure in RCFT.

In one comprehensive study that administered all the core subtests of the WAIS III/WISC III (4), they found that the AN group mean scores on the Processing Speed index fell in the *average* range according to the normative data. For the other tasks mentioned, no discussion of performance relative to the normative data was reported, with performances compared to healthy control groups.

Across the five studies that examined AN versus HC performances, none found significant differences in performances on Part A of the TMT (1, 4, 11, 14, 28). Samples in these studies were all comprised of females of a similar mean age and BMI, who were in treatment during the time of testing. However, Sarrar and colleagues (2016) did report that being in the AN group significantly increased individuals' chances of being in the lowest performing quartile on TMT A. Another study which examined possible confounds found that there was no relationship between TMT A performance and BMI (14). In the AN group, these researchers did find an association with brain-derived neurotrophic factor (BDNF), a protein that is expressed in brain regions responsible for higher cognitive and executive functions, whereby higher levels of this protein, implicated in neuronal survival and repair, were associated with reduced TMT A performance.

In contrast, the results for the other measures are less consistent. With regard to the time to copy measure on the RCFT, two studies found that their AN groups were slower than their HC groups (24, 11). However, the third only reported a trend towards differences, with performance on this task negatively correlating with grey matter volume in the AN group (30) during their initial admission. Additionally, two studies found no significant differences in AN group following weight gain when compared to the HC groups (11, 30). Interestingly two of these were mixed gender samples with

short duration of illness, but Andres-Perpina and colleagues' study (24) had a sample size roughly three times that of Lozano-Serra and colleagues' study (11). It may suggest that the other study was not sufficiently powered. Again, for the Digit-Symbol subtest of the Wechsler scales, there were inconsistent findings. Three studies reported no group differences (28, 33, 35) using the revised WAIS or WISC, while a fourth found the AN group performed worse than the HC group (1). Similarly, being in the AN group significantly increased individuals' chances of being in the lowest performing quartile in this study (1), like in TMT A. It is unclear whether the same versions of this subtest were used. Both studies found no significant differences in performance between AN and HC groups using Coding subtests (two different versions) before weight restoration (30, 33). Surprisingly, Bradley and colleagues (1997) found that at follow-up, the AN group performed better than the HC (33). This pattern was not observed in the other study, which reported no group differences in performance after weight restoration (30). In the three studies that used computerised versions of similar tasks that measured reaction times, all found significant between group differences. AN groups reacted more slowly than the HC group on the simple and choice reaction time task (4: CANTAB), visual set-shifting task (18: Amsterdam Neuropsychological Tasks Program (ANTP)) and choice reaction time task, and tapped less on their right hand (29: IntegNeuro battery) when tested while in treatment. These group differences in reaction time remained following weight gain in both studies (18, 29), but not for tapping speed on the right hand, where AN and HC performed similarly (29).

Looking in detail at the studies that compared AN groups' cognitive performance at different weights, processing speed tended to improve following weight gain (n = 4). One study reported improvements following weight recovery on overall cognitive performance (11), to the extent that their performance resembled that of the HC group, including that on processing speed subtests (RCFT and TMT A). This study

used an alternative version of the RCFT, called Taylor's Complex Figure Test for follow-up testing, thus reducing the risk of these improvements resulting from potential practice effects. Hatch and colleagues (2010) found that AN group tapped significantly more using their right hand (but not left hand), but no significant within-group differences in the choice reaction time task were found at follow-up (29). In the one study that examined TMT A following weight gain, significant improvements emerged (28). Interestingly, Bradley and colleagues (1997) found that AN performance improved relative to baseline performance on many of the neuropsychological tasks administered (33) to the extent that at follow-up, their AN group outperformed their HC counterparts in the Coding F's task. This suggests that the AN group's performance improved following weight increase, as there were no initial between group differences.

Attention

Studies that purported to investigate aspects of attention (n = 8; 4, 11, 14, 15, 29, 32, 33, 35) used a variety of tasks to investigate performance. These included: Rapid Visual Information Processing (RVP) from the CANTAB (4), TMT a (11,14), Switching of Attention, Sustained Attention, Go-No-Go and Auditory Oddball from the IntegNeuro test battery (29), Auditory Attention from the NEPSY-II (15), Digit Span and Coding from the Wechsler Scales (30), attentional subtests (9&10) of the PBS (32), and Dichotic Words and the Continuous Performance Test (33).

Overall, there were inconsistent findings across the tasks when AN group performance was compared to HC groups when underweight (n = 8). For the Colour-word Interference task that was employed in studies using the Ravello Profile, it was consistently reported that AN performance fell within the average range (3, 6, 16, 21). There were no between-group differences on the overall Attention/Executive functioning index score of the NEPSY II (15), with no differences in performance on

the auditory attention subtest. No significant between-group differences emerged for TMT A (11, 14) or for RVP (4), tasks that look more at undivided attentional speed. Looking at those studies that investigated selective attention (n = 4), two found no significant differences between groups using the Auditory Oddball task (29) and Dichotic Words (33). However, using the Digit Span subtest, another study found a significant difference with AN performing worse (30), while the other did not (35). With regard to sustained attention studies (n = 4), no differences were observed between groups using a range of measures, including the CPT (33), Coding subtest (30), Sustained Attention subtest (29) when compared to HC groups. In contrast, both attentional subtests of the PBS showed the AN group outperforming the PC group (32). The one study that investigated attention switching, using the IntegNeuro test battery found no differences at baseline (29).

In studies of weight-restored AN groups compared to HC groups (n = 3), again an inconsistent picture emerged. Despite finding only one significant between-group difference on all the attentional tasks administered at baseline (29), researchers found that the AN group outperformed the HC groups on the Sustained Attention and Switching Attention subtests of the IntegNeuro battery. Two other studies found no between-group differences at follow-up looking at similar aspects of attentional performance using the CPT (33), Digit Span and Coding (30).

When Hatch and colleagues (2010) compared underweight to weight restored performances in the AN group, they found that performance improved in Switching of Attention (29). No other study reported any findings from comparing baseline to follow-up AN performances.

Executive Functioning

Executive functioning (EF), encompassing inhibitory control, cognitive flexibility, decision making, planning and working memory abilities, was by far the most widely investigated neuropsychological domain in the studies under review. In total, 29 studies included a measure relating to executive functioning. Measuring executive functioning was deemed vital by the research team that developed the Ravello Profile (Rose et al., 2011), as executive dysfunction has been proposed as a potential endophenotype of EDs (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005). These abilities are widely considered to be the most likely candidate for cognitive impairments to be observed in individuals with AN. Looking first to more global indices of EF, Calderoni and colleagues (2013) reported no significant differences between AN and HC groups on the Attention and Executive index score of the NEPSY II (15). Stedal and Dahlgren (2016) reported on the executive functioning in a case series of males with AN. Despite wide variability in individuals' overall neuropsychological functioning, they found less divergence in scores on EF tasks, with these abilities falling broadly within the average range (3).

Inhibitory control. Studies that investigated inhibitory control (n = 11; 3, 8, 11, 15, 16, 19, 20, 21, 23, 24, 29) used similar types of tasks, involving the suppression of an over-learned response. Tasks included a Stroop task (11, 24), Verbal interference and Go-no-Go subtests from the IntegNeuro battery (29), Response Set and Inhibition from the NEPSY II (15), Colour-Word Interference from the Delis–Kaplan Executive Function System (D-KEFS) (3, 8, 16, 19, 20, 21, 23) and the Hayling Test (8, 20, 21). Stedal and colleagues (2012) found that their AN group scored within the average range on Colour-Word Interference subtests. Studies that examined cognitive inhibition (n = 5; 11, 15, 20, 24, 29) showed no differences between AN and HC groups when using

the Stroop task (11, 24), Verbal Interference subtest (29), Colour-Word Interference (20), Hayling (20) and Inhibition (15). However, the AN group did perform significantly poorer in Response Set (15) and Go-no-Go (29). When Frampton and colleagues (2012) divided their AN group into hypo and normally brain perfused (on the basis of a SPECT scan), they found that those who with hypo-perfusion performed significantly worse than the HC group on the Hayling Test (20).

Two studies investigated performance between HC and AN groups at follow-up following weight-restoration in AN groups (11, 29). No between-group differences were found at follow up in Lozano-Serra and colleagues' Stroop task (11). However, when they divided their AN group into menstruating and amenorrheic, they found that the amenorrheic group performed more poorly than either the menstruating or the HC groups on the Stroop task. This suggests the presence of menstruation is important to consider when investigating potential influences on cognition. Interestingly despite there being no differences between AN and HC groups at baseline, Hatch and colleagues (2010) found again that following weight gain, the AN group performed significantly better than the HC group in naming the colour of the word in Verbal Interference (29).

The above result is explained by further analyses that revealed significant within-AN group differences from baseline to weight-restored, due to improvement in Verbal Interference. Another study investigating within-AN group differences from acute to weight-restored states reported though that while performance improved after weight-restoration relative to baseline in AN group in Colour Word Interference, these within-group differences were not significant (16).

Cognitive flexibility. Cognitive flexibility is often measured by set-shifting type tasks, a domain that is thought to form part of the specific endophenotype of ED

(Tenconi et al., 2010). The Wisconsin Card Sorting Test (WCST; 1, 5, 7, 11, 13, 19, 24, 25, 26) and Trail Making Test (TMT B or condition 4 from D-KEFS; 2, 3, 4, 6, 8, 11, 16, 19, 20, 21, 23, 24, 35) were most commonly used to measure set-shifting ability in the studies under review (n = 21; 1, 2, 3, 4, 5, 6, 7, 8, 11, 13, 15, 16, 19, 20, 21, 22, 23, 24, 25, 26, 28). However, a range of measures were also used with this young population including: Animal Sorting from the NEPSY-II (15), the Visual Set-shifting Task from the ANTP (18), the Novel category learning task (22), the Brixton Test (6, 16, 19, 23), Intra-Extra Dimensional Set Shift (IED) from CANTAB (4, 26) and probabilistic Object Reversal Task (pORT) (1, 28). For those studies that compared AN group performances to normative data (n = 7; 4, 5, 6, 7, 16, 21, 23), most studies found that AN groups performed within the average range for the tasks, including WCST (5, 7), TMT (4, 6, 16, 21) and Brixton tasks (6, 16, 23). However, Stedal and colleagues (2012) did report that their AN group performed significantly worse than the normative mean on TMT B (23).

There were only differences observed between AN and HC groups performances in studies that used the WCST, oPRT and Visual Set-Shifting tasks to measure set-shifting abilities, but inconsistently. With all other set-shifitng tasks used in the studies under review (TMT: 2, 3, 11, 19, 20, 24, 35; Brixton:19; IED: 4, 26; & Novel Category Learning task: 22) non-significant findings were reported. The pattern of results for both WCST and pORT tasks were not consistent across studies. Four studies found that the AN group performed poorer on the WCST (5, 7, 13), one found that AN made fewer errors than HC, while performance between groups was similar in the other four (1, 11, 19, 24, 25). A further complication in understanding these inconsistencies is that is that different outcome measures were used in these studies to measure performance on the WCST. Overas and colleagues (2015) did investigate these results further, finding that AN group's weight-for-height ratio was positively correlated with both non-

perseverative errors and conceptual level responses (7). For pORT, the pattern was similarly inconsistent with one study finding that AN performed worse than that HC (28), while the other did not (1). Using the Visual Set-shifting task, Burhren and colleagues (2012) found that the AN group made fewer errors compared to the HC group, but had longer reaction times than them on shift versus non-shift trials, with no speed-accuracy trade off (18).

In two repeated-measures design studies which compared AN group performance following weight-gain/treatment to HC groups at follow-up, neither found a significant difference performance, using the WCST (11) and TMT (2). However, Burhren and colleagues (2012) found the same pattern of differences at follow-up (18), with the AN group continuing to perform slower, but more accurately, than HCs. In those studies that employed a within-group design (n = 4; 2, 11, 16, 18), two found that AN group's cognitive flexibility did improve following weight-gain when measured using the WCST (11) and TMT (2, 11). In addition, Buhren and colleagues (2012) also found that their AN group reacted more quickly on the visual set-shifting task after weight-restoration (18). Interestingly, there was no relationship between neuropsychological performance and weight in their sample (18). Dahlgren and colleagues (2013) reported improvements in their AN group on TMT and Brixton task, but these were not significant when compared to baseline (16).

Decision-making. One study employed a computerised version of the Iowa Gambling Task (10). This task is considered an ecologically valid measure of decision-making. They found that the AN group was impaired on multiple aspects of this task when compared to the HC group. However, their sample size was small, though it was comprised of matched pairs which increased power.

Planning. A number of studies employed a measure of planning abilities in their test batteries (n = 9; 3, 4, 6, 15, 16, 20, 21, 23, 29), including the Tower Task (3, 6, 16, 20, 21, 23), Stockings of Cambridge from the CANTAB (4), Maze and Timing subtests from IntegNeuro (29) and Clocks from NEPSY II (15). The group mean for performance on the Tower Task fell within the average range for all studies that used the Tower task (3, 6, 16, 21, 23). In studies that compared AN when underweight to HC groups (n = 4; 4, 15, 20, 29), none reported any differences in planning abilities using each of these measures in turn: Stockings of Cambridge, Clocks, Tower Task and Maze and Timing subtests. One study looked at performance in an AN group following cognitive remediation therapy, but performances following therapy completion did not improve significantly on the Tower task (16). This was echoed by the non-significant within-AN group differences in performance over time on both Maze and Timing tests following weight-restoration (29). However, consistent with their findings in other aspects of EF abilities, Hatch and colleagues (2010) did find that AN group performed better than HC groups following weight-gain in the Mazes task, but not in the Timing task (29).

Central Coherence. Weak central coherence is another aspect of neuropsychological functioning that has been proposed as forming part of the distinct cognitive profile of ED (Lopez et al., 2008). This involves a heightened focus on details than wholes when processing information. Ten studies examined this ability in their samples (2, 3, 4, 5, 6, 11, 12, 16, 21, 23). Kjaersadam-Telleus and colleagues (2015) found that the AN group scored significantly lower than HC on Perceptual Organisation Index score from the Wechsler scales (4; $p = 0.009$, with a small effect size of $d = -0.38$). Despite this difference, the AN group mean still fell within the lower end of the average range, obtaining a standard score of 93. Most commonly, studies derived a

central coherence index (CCI) score from the Rey-Osterrieth Complex Figure Test (RCFT) using various methods, (2, 3, 5, 6, 12, 16, 21, 23), often using that described by Booth (2006). Block Design from the Wechsler scales (11), the Group Embedded figures task (16) and the Fragmented Pictures task (5) were also used, as these tasks were deemed to measure aspects of local and global processing. It must be noted that there are no published norms for under 18s in terms of central coherence on some of these tasks, so studies used data from other studies using HC groups to compare AN performance against. This makes it more difficult to make accurate comparisons across studies. In the studies that compared AN performance to previously published normative research data (n = 6; 3, 5, 6, 16, 21, 23), most found that AN CCI scores on the RCFT fell within the average range (3, 5, 6, 16). However, Stedal and colleagues (2012) reported that in their mixed gender and older adolescent AN sample (mean age = 17.1 years), their scores fell significantly below the normative mean, though still within 0.5 SD of the mean (23). An important point was noted by Rose and colleagues (2012) who cautioned that in their specially selected small sample, there was a particularly wide range in AN individuals' CCI z scores, compared to other tasks (21). This may mean that researchers are not getting the full picture by only analysing cohort data at a group level.

When comparing to HC groups (n = 4; 2, 5, 11, 12), two studies that looked at CCI in the RCFT found no significant differences (2, 12), but another found the AN group scored significantly worse (5). There were no significant between-group differences found on Block Design (11), nor on the FBT (5). Two studies looked at performance in AN groups following CRT treatment, which specifically aims to improve these skills (2, 16). Following 10 sessions of CRT, vanNoort and colleagues (2016) found that AN groups improved relative to their own baseline results on the CCI, but suggest that the CCI is subject to practice effects as the HC group also improved

without any treatment (2). Another group also looked at the impact of CRT on central coherence using the CCI and the GEFT on an AN group. While they found a large within-group difference after CRT session on the GEFT (16; $p = 0.044$, $d = 0.77$), this was not present with regard to differences for the CCI index score.

Working Memory. Working memory is purported to involve both the short-term processing and storage of information (Baddeley & Hitch, 1974). Using third editions of age-appropriate Wechsler scales, Kjaersdam Telleus and colleagues (2015) found no difference in Working Memory Index (WMI) scores between AN and HC groups, and the mean WMI score for the AN group fell within the average range (4). Working memory was examined in both verbal and non-verbal domains in numerous studies (n = 6; 4, 10, 15, 29, 30 35). Versions of Digit Span from the Wechsler scales (30, 35) and IntegNeuro (29), Word List Interference from the NEPSY-II (15) and Symbol-Digit Learning Test (SDLT) (35) were used to measure verbal working memory (n = 5; 15, 29, 30, 35); while Span of Visual Memory from the IntegNeuro (29), Spatial Span and Spatial Working Memory subtests from the CANTAB (4), and an n-back task (10) measured visual working memory (n = 3; 4, 10, 29). Results using verbally-mediated tasks were variable. One study reported non-significant findings (35), another found that AN groups performed worse (30), while the last found that AN groups scored better on the reversed digit span task (29). The digit span task from the Wechsler scales scores both forward and reverse tasks together to develop an overall total score, while the IntegNeuro digit span task generates separate scores. Thus, it may be possible that this last pattern may have been observed in the first two studies, yet masked by being grouped with forward span task performance. Using the SLDT, Witt and colleagues (1985) found that their AN group performed worse than the PC, MC and HC groups, while non-significant findings were found using Word List Interference

(15). For visually-mediated tasks, no study reported any significant differences in visual working memory performance between AN and HC groups (4, 10, 20).

Two of these studies tested following increases in weight (29, 30). While AN remained better at reverse task performance compared to HC the second time round in one study following weight gain (29), in the other the between-group differences disappeared, suggesting that task performance in the AN group improved once weight-restored (30).

Verbal Fluency. While verbal fluency task performance taps into verbal abilities, these tasks also require executive control (Fitzpatrick, Gilbert, & Serpell, 2013). One third of the studies under review used a verbal fluency measure in their test battery (n = 12: 3, 6, 8, 15, 16, 17, 19, 20, 23, 27, 29). The Verbal Fluency subtest of the D-KEFS was the most commonly employed measure (3, 6. 8. 16, 17, 19, 20, 21, 23), with Word Generation from the NEPSY-II (15), Letter and Semantic fluency tasks from the IntegNeuro battery (29), Controlled Oral Word Association Test (COWAT) (24) and finally a Japanese language Word Fluency task (27). AN groups scored broadly within the average range for the verbal fluency task in three studies (3, 6, 16). One small case series reported an above average group mean score, with a scaled score mean of 13.78 (21). Though there was a wide range of scaled scores from 10-18 in this sample, and it must be noted that these individual profiles were chosen specifically to illustrate the wide variability in individuals' cognitive skills. In studies that compared AN groups to HCs, again an inconsistent pattern emerged whereby AN groups demonstrate significantly better verbal fluency abilities than HC groups in some studies (15, 17, 23), but not in others (19, 20, 24, 27, 29). When Calderoni and colleagues (2013) examined possible explanations for this result, they found that better semantic fluency was related to the presence of a mood disorder (15).

Hatch and colleagues (2010) compared AN to HC group performance following weight-gain in AN group (29). Despite finding no initial baseline differences, their AN group performed significantly better in letter fluency at follow-up. Following sessions of CRT, one team of researchers found that their AN group's letter fluency scores significantly improved, and that these were related to weight increases (16).

Visuospatial Ability

While visually-mediated tasks were often used to measure various other cognitive domains, some tasks were used to specifically examine aspects of visuospatial ability in seven studies (4, 12, 15, 20, 24, 30, 33). Calderoni and colleagues (15) investigated visuospatial ability using the NEPSY II, and found that there were no significant differences between AN and HC groups in the Visuospatial processing index scores. Tasks that were used in this review include: accuracy of copy in the RCFT (4, 12, 24), Silhouettes from the Visual Object and Space Perception battery (20), Block Design from the Wechsler scales (30), Arrows, Block Construction, Design Copying, Geometric Puzzles, Picture Puzzles and Route Finding from the NEPSY-II (15), Visual Search Test (33), Mental Rotation Task (33), Judgement of Line Orientation (33), Card Rotations Test (33), and Perceptual Closure Test (33). AN and HC groups performed similarly on the Silhouettes task (20), all of the visuospatial subtests from the NEPSY II (15), and all the visuospatial tasks in Bradley and colleagues' (1997) study. With regard to the accuracy of copy measure of the RCFT, in two studies AN groups were significantly more accurate than their HC counterparts (4, 12), but not in the third (24).

Verbal Abilities

Examining verbal abilities was rarely the focus of the studies under review. Instead, verbal tasks were often administered as part of deriving a measure or estimate

of global intellectual functioning with fifteen studies including a verbal task in their battery (4, 6, 7, 8, 9, 11, 13, 15, 17, 21, 23, 30, 31, 32, 36). Most commonly, the Vocabulary (4, 6, 7, 8, 9, 11, 17, 21, 23, 30, 36) and Similarities (4, 13, 30, 36) subtests of the Wechsler scales (various editions of the WAIS, WISC and WASI) were administered, along with the Vocabulary subtest from the CFT battery (31), Verbal subtests 1, 2, 5 & 6 from the PBS (32), and Comprehension of Instructions, Oromotor Sequences, Phonological Processing, Repetition of Nonsense Words, Speeded Naming & Word Generation subtests from the NEPSY-II (15). In studies that reported the AN group means on the Vocabulary and Similarities subtests (n = 12; 4, 6, 7, 8, 9, 11, 13, 17, 21, 23, 30, 36), all obtained scores that fell within the average range according to normative data. The AN group also obtained an average score in the Language index scores of the NEPSY-II (15). There were no significant differences between AN and HC groups on verbal abilities (n = 4), either when underweight (7, 17, 30, 31) or following weight-restoration (30, 31). However, two older studies did find that AN groups scored significantly higher than PC on verbal abilities (32, 36). Neumarker and colleagues (2000) also did not find any significant differences between baseline and follow-up performances after weight-gain on the vocabulary battery (31).

Memory

Verbal memory. Five studies measured verbal memory skills (4, 15, 24, 29, 33), using tasks that used immediate and delayed, cued and free recall and recognition conditions. These included: Memory for Stories - Immediate and Delayed subtests from the Tests of Memory and Learning 2nd Edition (4), List Memory, Memory for Names, Narrative Memory and Sentence Repetition under all conditions from the NEPSY II (15), Verbal Learning and Recall from the IntegNeuro test battery (29), Logical Memory I&II from the Wechsler Memory Scales (24), Rey Auditory Verbal Learning

Test (RAVLT) - immediate recall (24) and Verbal scales from the Denman Neuropsychological Memory Scales (33). Again, results varied across the tasks used. There were no significant differences between AN and HC groups found in the NEPSY II verbal memory subtests (15), immediate and delayed Logical Memory I&II subtests and immediate RAVLT scores (24), and in the Word Selective Reminding task (4). In the immediate condition for the Memory for Stories subtest, the AN group remembered less than the HC group but similarly on the delayed recall task (4). In the Verbal Recall task, AN group scored significantly worse than HC (29). After weight-gain at follow-up, this AN group performed worse on Memory recognition than HC, they performed better on memory recall (29).

Visual Memory. More studies under review investigated visual memory skills (n = 14; 3, 4, 6, 11, 12, 15, 16, 20, 21, 23, 24, 30, 33, 35), possibly because the RCFT featured as part of the Ravello Profile, looking at both immediate and longer-term memory conditions. Tasks that were used included: immediate and delayed recall measure of RCFT (3, 6, 11, 12, 16, 20, 21, 23, 24, 30), Pattern Recognition Memory and Spatial Recognition Memory (4), Visual Reproductions - immediate and delayed conditions from the Wechsler Memory Scales (11, 24, 35), Memory for Designs and Memory for Faces - immediate and delayed recall conditions from the NEPSY II (15), and the Nonverbal Scale of the Denman Neuropsychological Memory Test (33). With regard to how AN groups' abilities were ranked according to normative data for the RCFT, the most commonly employed task, all AN group means fell within one standard deviation of the normative mean (3, 6, 16, 21, 23). Stedal and colleagues (2012) did report though that their AN group mean still fell significantly below the normative mean. Another study found that following treatment, immediate and delayed recall performance improved in the AN group when compared to initial assessment on RCFT

(16). This improvement was significantly related to weight-gain. In contrast, Rose and colleagues (2012) found no significant differences in recall performance in both conditions between their underweight and weight-restored AN participants (21). Castro-Fornieles and colleagues (2009) found no significant between-group differences following weight-gain either (30).

AN (in treatment) and HC groups' performances performed similarly on all the visual memory tasks, other than the RCFT (4, 11, 15, 24, 29, 35). The picture relating to immediate and delayed recall performance on this task was less clear-cut. Of the five studies that compared AN and HC groups, four reported no significant between-group differences on the RCFT memory measures (12, 20, 24, 30). The last did find that AN groups recalled less on immediate recall, but no significant differences were found on delayed recall (11). Interestingly, when Frampton and colleagues (2012) subdivided their early-onset cohort into hypo and normally neurally perfused, they found that the hypo-perfused group performed worse than normally perfused AN and HC groups on the delayed condition of the RCFT (21).

Academic ability

Academic skills are underpinned by multiple cognitive domains. However, given that tests of academic attainment are often included in neuropsychological assessments in this age group and correlate highly with them, it seemed pertinent to mention those two studies that included a measure of academic attainment in this review (13, 34). This also has merits with relation to understanding the broader clinical picture of adolescents with AN, given the many clinical anecdotes of their high levels of scholastic achievement. Both studies used various editions of the Wide Range Achievement Tests (WRAT) to measure this. Both found that AN groups scored within the average range on the reading subtest (13, 34). In the older study, researchers found

that their AN group scored within the average range on the Arithmetic subtest too, but in the high average range on Spelling (34). Their AN group also scored higher than their VIQ and PIQ predicted on both Reading and Spelling. Wiereng and colleagues (2014) found that there were no significant differences between AN and HC groups on the Reading subtest (13).

For an overview of all the domains along with the test batteries and tasks used to measure performance across the studies, please see Appendix II.

Discussion

To our knowledge, this is the first systematic review of the literature to specifically examine the broad neuropsychological profile of adolescents with AN using strict age criteria to ensure that the majority of the sample are adolescents. Its aim was to synthesise and critically review the 36 peer-reviewed studies that examined aspects of the neuropsychological profile of adolescents with AN. This review provides an overview of performance across multiple domains of functioning including: intelligence, processing speed, attention, multiple aspects of executive functioning, visuospatial abilities, verbal abilities, memory (verbal and visual) and academic abilities.

The vast majority of studies were of reasonable quality, being rated as either "medium" or "high" quality according to the criteria employed. Studies under review commonly employed a cross-sectional design. These mostly included female AN participants who were in treatment at the time of testing and still underweight according to their BMI. Their neuropsychological performance was often compared to a group of similarly aged healthy controls. However, a wide range of research designs and methodologies were employed across the studies, with many differences with regard to

age-range, BMI and illness duration. There were also variations in how potential confounding variables, such as co-morbidities and psychoactive medication, were treated in the design and analyses. These design and methodological inconsistencies in the evidence base have previously been described as problematic (Lang et al., 2014; Lask & Bryant-Waugh, 2013; Reville et al., 2016). As previous authors have noted, the conclusions drawn from this evidence as a whole are limited due to methodological differences (Jáuregui-Lobera, 2013; Tchanturia, Campbell, Morris, & Treasure, 2005). There are additional challenges when making comparisons across the heterogeneous tasks used to examine each cognitive domain, and having to consider that different outcomes measures reported even when the same task was used. Given these issues, it is pertinent to consider the utility of adopting the approach of the researchers behind the Ravello Profile project who have addressed these challenges by developing a standard test battery for investigating neuropsychology in AN (Rose et al., 2011). Their influence was noted in the studies under review.

Overall it would seem that the results of this review together indicate that there are no gross, absolute neuropsychological impairments in adolescent AN. There may well be subtle impairments relative to the level expected of the individual on the basis of optimal/premorbid functioning, but these may have been missed in the group studies. These results are in agreement with the general consensus of previous reviews of adult functioning (Tchanturia et al., 2005). Differences when AN groups were compared to healthy adolescent groups across all measures, if present, tended to be subtle. AN group means across all measures tended to fall within the average range according to normative data. It must also be noted that there was little discussion of clinically, as opposed to statistically, significant change in the studies under review, with many older studies not reporting effect sizes. This makes it hard to estimate the relative clinical importance of their significant findings. Therefore, even if impairments relative to

normative data or HC groups were found in AN groups, it is difficult to know whether these would be significant enough to impact on their daily functioning. One of the important evolutions in this field is the publication of case series of individuals' cognitive profiles, as opposed to reporting only on a group level basis. These studies indicated the wide variety in performances across domains that exist (e.g. 3, 6, 21). Some authors have cautioned that only using group level data analyses may mask huge individual variation (3), which would be important to be aware of in clinical settings.

Some recent studies found that various physical and psychological characteristics within AN groups did have a relationship to their cognitive functioning aside from weight-gain. These included the presence of amenorrhea even when weight-gain was achieved (11), the degree of perfusion through the brain (20) and symptoms of low mood (15, 16). This indicates that it would be important to consider the influence of factors beyond just weight-gain, when seeking to understand the cognitive profile presented in repeated-measures designs. Previous authors have also cautioned that recovery from AN must not simply be construed as weight restoration by researchers, as other factors such as the absence or reduction of associated behavioural and psychological factors should also be taken into account (Bardone-Cone et al., 2010). While one study under review here found that significant improvement in depression scores explained better performance on a central coherence task (16), another found that the presence of a mood disorder was related to better semantic verbal fluency (15). A recent review of the impact of depression on neuropsychological performance in AN, concluded that only a minority of studies control for depression in their analyses despite widespread measurement of symptomatology (Abbate-Daga et al., 2015). Their analyses found two studies did report that the greater the depression score, the more impaired performance on neuropsychological tasks; however, most studies did not find that depression scores explained the difference between AN and HC group performances.

There is also considerable evidence from the depression literature itself that depression on its own has an impact on neuropsychological test performance, particularly with regard to executive functioning (Snyder, 2013). Thus, it is important to consider the impact that depression symptoms may have on performance in this group. This is important as the influence of depression on functioning in AN is still not well understood despite frequent measurement, with inconsistent results reported in the few studies that have considered its potential effect.

AN group mean scores across all tasks in all neuropsychological domains fell within the average range according to normative data across all the tasks used. In studies that examined skills before and after weight-gain, many found that performances across domains assessed tended to improve to some degree, but did not always reach statistical significance, suggesting that these improvements were subtle if present. Inconsistencies were often present when comparing results across studies, even when similar tasks were used. This may be explained by differences in sample size, age of sample, duration of illness and numerous other confounds. Mostly, AN groups tended to perform similarly to healthy adolescent control groups, with at least half of studies reporting non-significant findings when they were compared within each domain. Only in the area of verbal fluency did the AN group tend to occasionally outperform their healthy counterparts, whereas in most other domains if differences were present they tended to perform worse, for example displaying poorer set-shifting abilities on certain tasks.

With regard to overall intellectual functioning, all studies reported that AN group means fell within the average to high average range, with the majority reporting no significant differences in performance with healthy adolescent controls. These results are in broadly in line with the findings of a meta-analytic review that examined intellectual functioning in studies that used the National Adult Reading Test and

Wechsler Intelligence Scales in both adolescents and adult samples (Lopez, Stahl, & Tchanturia, 2010). They reported that AN participants' group mean scores were slightly higher than the average normative score, but still fell within the average range. They also found that participants tended to have higher IQ scores when recovered, which is in agreement with two of the studies here under review, who reported that IQ improved following weight-gain relative to baseline (28, 31). Given the often noted clinical phenomenon that individuals with AN tend to do very well academically, it was notable in the studies under review here than one study found that adolescents scored higher on certain tasks of academic attainment than their IQ would predict (34). These authors proposed that high levels of trait perfectionism may be responsible for this (34). It is also important to note that there are inherent difficulties in using proxy measures of IQ, which tend to perform poorer at the tails of the distribution. This phenomenon may be relevant to many of the studies reviewed here that used proxy measures, given they have been noted to underestimate IQ levels at the upper end of the spectrum. (Spinks et al., 2009).

Similarly, when looking at processing speed and attention tasks, AN groups scored within the average range according to normative data. There were no differences in performance between clinical and control groups across most tasks used for both domains, with only computerized testing batteries consistently finding AN completing processing speed tasks more slowly than HC groups. Processing speed and attention tended to improve following weight-gain in AN groups. One could speculate that computerized testing batteries may be more sensitive to the subtle impairments likely to be seen in AN groups; however, research is required to test this hypothesis using comparable pen and paper, and computerized tasks. For both visuospatial and verbal abilities, most studies found that AN and HC groups performed similarly across the range of tasks used, but two older studies did find that their AN groups demonstrated

better verbal abilities than the PC groups. Mixed findings were reported on verbal memory task performance, with around half of the studies reporting no differences between AN and HC groups, and the others reporting poorer performance in AN groups. Nearly all studies reported AN and HC groups performed similarly on a range of visual memory tasks, with most studies not finding any improvements following weight gain in AN groups. This suggests that visual memory domain may be less affected by weight fluctuations. With regard to academic ability, only a couple of studies investigated this, finding that AN attainment fell broadly within the average range. Although, one study did report that certain academic skills were higher than their reasoning skills would have predicted.

Looking at executive functioning, individuals with AN performed within the average domain on both global indices of functioning and within sub-domains. With regard to inhibitory control and planning, most studies found no differences between AN and HC performances. The one study that looked at decision-making did find that their AN group performed more poorly than HC, and may indicate the benefit of using more ecologically valid tasks to assess ability. Inconsistent findings emerged for tasks that purported to assess working memory and verbal fluency when comparing AN and HC groups. However, three studies did find that AN groups when underweight outperformed HC groups, and performance further improved following weight gain, as it tended to in working memory tasks also. This suggests that performance in these domains may be affected by weight status (i.e. degree to which someone is underweight), which may explain the inconsistencies in findings as groups' mean BMI/weight-for-height differed, and may even be an area of strength for young people with AN.

Moving specifically to the set-shifting tasks, the WCST and TMT that were used as measures of cognitive flexibility in our review, it is pertinent to consider the results

of a recent meta-analysis of set-shifting abilities in young people carried out by Lang and colleagues (2014) that included many of the same studies. They concluded that that there were no significant differences between AN and HC groups in performance on both these tasks. While our review included a broader set of nine tasks, only three tasks demonstrated any impairments in AN groups relative to HCs (WCST, pORT and Visual Set-shifting task). Even within these tasks, inconsistencies emerged, with some studies finding differences and some not. Findings were also inconsistent with regard to the impact of weight gain on set-shifting performance, unlike in other domains, with some findings improvements and some not. This may suggest that the influence of weight (i.e. a state characteristic) may be less related to set-shifting abilities in adolescent AN groups. When Lang and Tchanturia (2014) reviewed central coherence in young people, they concluded that there was evidence to suggest that AN groups show less globally orientated processing in central coherence tasks. However, again they noted it was difficult to draw firm conclusions due to methodological inconsistencies. In our review, again inconsistent results were found across the nine studies that examined central coherence. Furthermore, it was difficult to bring clarity to these results given the lack of standardized normative data for younger populations' performance on many of these central coherence measures.

Limitations of current review

The inclusion criteria precluded studies that used experimental tasks from being included in this review. Neuropsychological tasks have often been designed to detect gross impairments in functioning in patients with neurological conditions, as opposed to mental health conditions. Therefore, these tasks may not be sensitive enough to detect subtle difficulties or strengths in these profiles that may provide more clues as to the neuropsychological profile.

Only including studies published in the English language resulted in some seemingly relevant studies being excluded from this review. This could have further broadened our understanding of the current literature base.

It must also be noted that there is a lot of debate surrounding both the ecological validity of neuropsychological tasks, including both the tasks themselves and the conditions in which they are administered (free of distraction), which are far removed from real-world demands (Stedal & Dahlgren, 2015). Neuropsychological tasks, although standardised, were primarily designed to be used in neurological settings, rather than with psychiatric patients. Thus, many may not be sensitive enough to detect subtle impairments. This may mean that adolescents with AN may still struggle with aspects of their daily functioning due to cognitive difficulties, even if their neuropsychological profile does not demonstrate any major impairments. Therefore, by not including studies that used self-report measures of neuropsychological functioning in this review, we may have excluded studies that could have shed further light on the perceived daily functioning of young people with AN by both their parents and themselves. And thus, failed to better understand the relationship between direct and self-report measures of neuropsychological functioning in this group.

Clinical Implications

There is currently no clarity regarding the relationship between AN and neuropsychological functioning in adolescence given the numerous methodological differences and inconsistencies in the results of the studies under review. Certainly at a group level, the evidence base suggests that there are no gross deficits in the neuropsychological functioning of adolescents with anorexia. Therefore, for clinicians working with young people with AN, conducting direct neuropsychological assessments for all their young clients as a matter of routine would not be warranted. Clinical

judgment should be used to inform the need for direct testing on a case-by-case basis, based on the information gained from clinical interview with the young person and their families.

There may be a broad range of functioning within AN groups in adolescence, as evidenced by the case series included in this review. Clinicians should enquire at assessment about any changes noticed in cognitive functioning since the onset of AN, or if the young person and/or their families has any longstanding concerns about their cognitive functioning, as pre-morbid deficits may exist. However, it would not be possible to know if any pre-morbid deficits present were necessarily related to the presence of AN or not. If any concerns are reported and testing is clinically warranted, a measure of pre-morbid intelligence should be included within their assessment battery, as physical changes resulting from AN (e.g. amenorrhea) and weight-restoration have been shown to influence to cognitive functioning. This may suggest if the young person's functioning has significantly changed following the onset of AN, and depending on their stage of recovery, the possibility that certain domains may improve following a return to physical and psychological health (e.g. working memory, verbal fluency). Clinicians must also be aware that the presence of common co-morbidities, such as depression, may also influence cognitive functioning, and so must not be ignored at assessment and when designing interventions. As with all neuropsychological assessments, these results can then be used to help inform the formulation of the presenting difficulties, and from that the interventions warranted for that individual.

Recommendations for future research

Research continues to examine the questions posed in the review at a rapid pace, with three relevant studies published in the two months following the search completion. It is vital that researchers collect and report sufficient details regarding the

state of their AN sample to contextualise the findings, especially with reference to age of onset of AN, duration of AN, presence or absence of psychoactive medications and co-morbid diagnoses. As Essie and Eisler (2015) recently commented in their review of the literature, there is still a profound lack of understanding of the role of co-morbidities in the current evidence base. Therefore, it is recommended that AN individuals presenting with these potential confounding variables be included in studies, in order to determine their relative influence, if any, on their neuropsychological profiles through statistical analyses. This will also have the added benefits of helping increase the sample size and making samples more representative of the typical AN adolescent population. If individuals are in treatment during testing, the content of this treatment should be described, i.e. whether this treatment is purely weight restoration focused, or if psychological approaches are included. It should also be stated clearly at what point in their illness they participated: at initial diagnosis, after weight-restoration or following complete recovery. Furthermore, given the known cognitive impact of acute fasting states in healthy individuals in certain domains, most often EF (Benau, Orloff, Janke, Serpell, & Timko, 2014), it would also be important to give an account of the approximate calorie intake on the day of testing. Only one study under review made reference to this in very vague terms (13), as differences in calorie intake may well further contribute to subtle differences noted in AN samples.

With regard to test selection, it is clear that a wide selections of tasks are currently used in research. It is pertinent that researchers make efforts to ensure that their test batteries have previously demonstrated sufficient sensitivity in the cognitive domain they are looking to examine in psychiatric samples, as opposed to neurological samples. Given that it is likely that differences will be subtle at the group level if present, these tests must be sensitive enough to detect small effects (Stedal & Dahlgren, 2015). Future researchers should make efforts to standardise some of the tasks used in

experimental studies that have already be found to be better suited to detecting small effects in typically developing healthy populations. These may be better suited to assessing functioning in psychiatric populations.

A test for overall intellectual functioning should always be included in the test battery, unless the test under use is co-normed with an IQ test. Otherwise, it is difficult to judge the relative strengths or weaknesses in AN samples, as it may likely that overall IQ score may be slightly higher than average in this population.

Further research should include mixed gender samples and make efforts to recruit male adolescent participants. Although it is widely accepted that a higher proportion of females suffer from AN than males, males also develop AN, and there is currently a severe lack of research into the cognitive profiles of males with AN. In addition, this may facilitate the investigation of any gender differences present in the neuropsychological functioning in AN samples, as there are known sex differences in neural development (De Bellis et al., 2001) and in performance on neuropsychological tasks (Baron-Cohen, Knickmeyer, & Belmonte, 2005) within the general population.

Recent research has already begun to focus on the neuropsychological profile of children at high risk of developing AN, as the potential genetic basis to this serious mental health problem is now better recognised. Kothari and colleagues have assessed children of mothers with lifetime AN, and suggested that these children display difficulties in visual-motor functioning, planning and reasoning, along with social understanding when tested at 4 years, 8 years and 10 years (Kothari, Rosinska, Treasure, & Micali, 2014; 2013). These authors suggest that these types of difficulties, which also relate to difficulties displayed by individuals with AN, may indeed be pre-morbid. However, the results of this review did not reveal such clear evidence as to eliminate the possibility that subtle impairments evident may be state related also, as weight-gain often improved performance. Given the need to better chart the

developmental course of AN on neuropsychological functioning and to determine whether the aspects of these profiles are state or trait, it would be pertinent to conduct research using the same methodology and more comparable measures in adolescent and adult AN samples to allow for more accurate comparisons.

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Part 2: The Empirical Paper

To Fast or not to Fast: The impact of the 5:2 diet on Cognitive Functioning in Healthy Adults

Abstract

Aims

Understanding the relationship between nutrition and cognition has been informed by two evidence bases. Studies have shown that cognitive functioning in healthy adults in negatively impacted by acute fasting states. In addition, there is also growing evidence to suggest a specific cognitive profile associated with eating disorders (ED) exists, but whether these cognitive deficits are pre-morbid vulnerabilities or whether extreme caloric restriction may contribute remains unclear. With the growing popularity of intermittent fasting diets, little is known about the impact of these diets on cognitive functioning to inform potential dieters. This study sought to understand the impact of one such diet, the 5:2 diet on cognition in healthy adults.

Method

This within-subjects prospective study examined the influence of intermittent fasting on cognitive tasks over 1 month, using the popular 5:2 diet. This diet involves restricting calorie intake to a quarter of typical intake on two days per week. Healthy adults beginning this diet were recruited worldwide, and acted as their own control. After practicing the diet for 3-4 weeks, their cognitive performances on a series of online tasks were compared on a fasting versus non-fasting day. We specifically investigated their prospective and working memory, impulsivity, set-shifting and psychomotor abilities ($n = 74$).

Results

Results from mixed between-within linear models indicated no significant differences in performance on fasting over non-fasting days on any task ($p > 0.05$),

suggesting that restricting calorie intake did not influence participants' executive function abilities enough to affect their performance on these tasks.

Conclusion

These results differ from the pattern observed in previous studies that have found impairments in executive function abilities in healthy adults when fully fasted. This suggests that perhaps even minimal calorie intake may have a protective impact on cognitive performance in the short-term. Given the high dropout in the wider study before the completion of both sets of tasks, there may have been sampling biases. These could explain the lack of significant findings. Further research incorporating incremental calorie intake designs may aid understanding of the observed cognitive deficits in ED and the inconsistencies in previous studies' results. This is especially relevant given the delicate balance observed in animal studies between calorie intake and functioning. The study does not provide evidence for the view that intermittent fasting leads to cognitive deficits on fasting days.

Keywords

Intermittent Fasting - 5:2 Diet - Healthy Adults - Cognition - Executive Functioning

To Fast or not to Fast: The impact of the 5:2 diet on Cognitive Functioning in Healthy Adults

Researchers have long been interested in the relationship between nutrition and human cognition. One of the seminal studies in this field was the Minnesota Starvation Experiment that was carried out by Ancel Keys and colleagues during World War II (Keys, Brozek, Henschel, Mickelson, & Taylor, 1950). It was designed to educate the American government on how best to treat the likely effects of poor nutritional intake on civilians during the war (Kalm & Semba, 2005). Most recently, there has been an upsurge of interest in the idea of calorific restriction for longevity (CRL). Proponents of this view claim, based on animal model studies, that through chronic under-eating (typically 40% reduction on typical calorie intake) with adequate micro-nutrient intake, individuals can benefit from prolonged health and increased lifespan (Vitousek, 2004). There have been suggestions from the literature that calorific restriction can improve human cognition and reduce rates of dementia given promising results from many animal-based studies, though the research evidence in humans remains inconclusive (Dirks & Leeuwenburgh, 2006; Martin, Mattson, & Maudsley, 2006). Some observational population-based human studies have suggested a potential relationship between reduced calorie intake and decreased rates of dementia (Luchsinger, Tang, Shea, & Mayeux, 2002; Willcox et al., 2007). However, results from randomised controlled trials (RCTs) have been mixed. Some have reported improvements in verbal memory function from reducing calorie intake (Witte, Fobker, Gellner, Knecht, & Flöel, 2009), but others have failed to find any changes across numerous neuropsychological tasks (Martin et al., 2007). The possibility of caloric restriction being protective against dementia is particularly of interest to neurocognitive researchers given the increase in

such conditions, like dementia, in our ageing society and their associated burden of care (Smith & Blumenthal, 2010) and their impact on wellbeing.

Given the interest in the potential benefits to human health and cognition from reducing calorie intake, a number of dietary practices have been developed to harness these effects. One such practice is intermittent fasting (IF), which is more easily adhered to than the strict daily regime required by CRL. The increasingly popular 5:2 "Fast" diet utilises IF, instructing individuals to severely reduce their calorie intake on two days per week (600 for men, 500 for women), while eating normally for the remaining days (Mosley & Spencer, 2013). This diet claims to help people lose weight, while also improving overall health and wellbeing; but the research evidence underpinning these claims in humans is in its infancy.

IF diets are purported to work by changing (i) cellular stress response systems, and (ii) energy and oxygen radical metabolism, in ways that protect neurons from falling prey to known genetic and environmental factors that occur during the aging process, such as an age-related decline in peroxisome proliferator-activated receptor, a transcription factor that regulates the expression of genes (Martin et al., 2006). This type of dieting has been reported as being at least as effective as modest daily calorie restriction with regard to overall health benefits, including weight-loss, improved insulin sensitivity and other biomarkers of health (Brown, Mosley, & Aldred, 2013). However, most studies of IF so far have included obese participants and have examined its effects on specific physical health benefits, such as changes in biomarkers for diseases (e.g. Harvie et al., 2010). It currently remains unknown what effect the 5:2 diet has on cognition - either in the short or long-term. If potential dieters are to make informed decisions, it would be pertinent to determine what, if any, impact reducing calorie intake would have on cognitive functioning on fasting days. This would further inform interested individuals about the actual risks and benefits of this diet.

While the impact of IF on cognition remains unknown, the body of evidence investigating the relationship between fasting and cognition is better developed. In short-term fasting regimes in adults, research has shown that moderate hyperketonemia occurs (Bouteldja, Andersen, Møller, & Gormsen, 2014), suggesting that the brain may be using alternative sources of fuel to glucose (its main source) in order to maintain neural functioning during times of nutritional stress as glucose levels decline. One study using positron emission tomography has shown that in four obese adults, glucose levels fell uniformly throughout the brain after a three week fast (Redies et al., 1989). Benau and colleagues (2014) have recently published a systematic review of ten studies that investigated the impact of short-term fasting on numerous cognitive skills in healthy adults. Their analyses revealed inconsistent results across the studies; however, some studies did find that tasks involving executive function, psychomotor speed and mental rotation skills were affected to some degree by fasting. The authors did note that there is a need for further well-designed studies to be conducted, given the inconclusive nature of their results and the many confounding variables in the research designs. Within our current research group, more recent short-term fasting studies have demonstrated an impact on set-shifting tasks, an aspect of cognitive flexibility (Bolton, Burgess, Gilbert, & Serpell, 2014), as well as on a response inhibition task, specifically looking at reflective impulsivity (Howard, Gilbert, Burgess, Dayan & Serpell, unpublished). These skills are both aspects of executive function, an umbrella term used to describe a set of "general-purpose control mechanisms" that regulate the interplay between human cognition and action, and are often associated with the prefrontal cortex of the brain (Miyake & Friedman, 2012).

Alongside research into the effects of CRL and IF on humans, another body of evidence has been accumulating from those investigating atypical eating patterns in the clinical field of eating disorders (EDs) (Vitousek, Gray, & Grubbs, 2004). Clinicians

have long been interested in understanding the psychopathology of individuals presenting with EDs in order to determine how best to prevent and treat them. Research focusing on the cognitive functioning of individuals suffering from EDs has identified specific areas of deficits that have been consistently implicated, including aspects such as set-shifting, central coherence, visuospatial and visual memory skills (Stedal, Rose, Frampton, Landro, & Lask, 2012). However, given the complexities inherent in research using clinical ED samples, it is difficult to determine whether the pattern of deficits observed are pre-morbid vulnerabilities or whether they resulting from prolonged disturbed caloric intake patterns (Benau et al., 2014). This is especially true for set-shifting, as deficits in this area have been observed in both affected and unaffected sister pairs when compared to healthy controls (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005) and while deficits remain, they reduce in degree following recovery (Treasure & Schmidt, 2013). Set shifting abilities have been linked with specific neural structures, such as the medial prefrontal cortex and anterior cingulate cortex in fMRI studies (Bissonette, Powell, & Roesch, 2013). Impulsivity (resulting from poor response inhibition) has also been implicated as a risk factor for developing an ED, and a recent systematic review concluded that individuals with EDs, particularly those with a binge/purge subtype, have demonstrated more impulsive behaviours than healthy controls (Waxman, 2009). In a recent review, Bari and Robbins (2013) proposed that it was likely that interaction between the inferior frontal cortex and the pre-supplementary motor areas of the brain that facilitates the inhibition of a pre-planned motor response.

Given that inducing chronic states of starvation in healthy individuals raises great ethical concerns, and the risks it would pose (Jones, Duncan, Brouwers, & Mirsky, 1991), researchers have advocated for the use of experimental short-term fasting studies in healthy adults (12-48 hours). This alternative design may provide further insight into

unpicking the pre-morbid cognitive risk factors from the resulting effects of reduced calorie intake on the brain and, consequently, cognitive function in individuals with EDs (Benau et al., 2014). Executive skills, such as cognitive flexibility and response inhibition, have both been identified in the current evidence base as having been affected by short-term fasting in healthy adults, though more research is needed to determine the replicability of findings. These aspects of executive functioning have also been implicated as being risk factors to developing an eating disorder. Set-shifting difficulties, an aspect of cognitive flexibility, have been found in individuals with anorexia nervosa (AN), their unaffected sisters (Tenconi et al., 2010) and their unaffected first-degree relatives (Galimberti et al., 2013). By determining the distinct differences and similarities in the cognitive profile of fasting in healthy individuals from individuals with EDs, clinicians may be able to better tailor treatment programs. For an example, if it was known that working memory was both negatively affected by fasting states in healthy individuals and in individuals with AN, one might expect working memory to resolve upon weight-restoration and adequate calorie intake. Therefore, until recovery is achieved, additional supports may be required to support functioning. This is vital given the need to determine what factors may help promote recovery (Kinoy, 2013). Therefore, through the use of an experimental paradigm to look at the impact of IF on executive functioning tasks in healthy adults who are following the 5:2 diet, it may be possible to aid the understanding of those cognitive factors that predispose ED and those resulting from the effects of insufficient calorific intake. However, it is recognized that the 5:2 diet is not considered a model for any eating disorder.

Given the current paucity of research investigating the impact of the 5:2 diet on cognition, it would be important to determine what these cognitive effects are, given the popularity of this diet. IF diets, such as the 5:2 diet, are being marketed as diets that will not only improve your health and wellbeing in the short-term, but will prolong your

lifespan and potentially reduce the risk of neurodegenerative diseases (Martin et al., 2006). However, it would be important to consider the impact of the 5:2 diet on cognition, particularly executive functioning, given the reported results in the short-term fasting literature in healthy adults and knowing that executive functioning deficits are also observed in individuals with EDs, whose calorific intake may often be greatly restricted but not entirely. This raises questions about the potential negative cognitive impact for individuals who are severely restricting their calorie intake on two days every week while undertaking the 5:2 diet. An additional consideration when considering potential risks is that dieting is an often cited risk factor for developing some types of EDs, due to nutritional stress occurring in the context of a life event, (Southgate, Tchanturia, & Treasure, 2005) and other weight-related conditions (Haines & Neumark-Sztainer, 2006).

Therefore, this study proposes the following hypotheses:

1. There will be a change in healthy adults' performance on specific cognitive tasks, including cognitive flexibility and response inhibition, from fasting to non-fasting days when engaged in the 5:2 diet, with poorer performance on fasting days.
2. Healthy adults engaged in intermittent fasting will exhibit a similar pattern of performance on different executive tasks on fasting days as individuals with EDs.

Methodology

Participants

A healthy adult sample (male and female aged between 18-65 years inclusive) were recruited for this study worldwide (n = 177). This online study sought to recruit individuals who had already decided to embark on following the 5:2 diet, but had not

yet started implementing the regime. Recruitment was achieved through advertising on university/research volunteer databases; placing adverts in public community buildings; through word of mouth; posting on relevant online platforms, including the official 5:2 diet forum (https://thefastdiet.co.uk/forums/) and a running forum (http://www.fetcheveryone.com/forum.php); and social media platforms, using a study-specific Twitter account (see Appendix V for recruitment poster). We sought permission from relevant authority figures prior to posting adverts in all domains. Our main source of participants came from the online 5:2 diet forum.

Participants were eligible for participation if they were aged between 18 and 65 years old, fluent English speakers with normal or corrected to normal visual acuity, computer literate with internet access, and were about to embark on the 5:2 diet. Exclusion criteria included: any current or previous history of an eating disorder, any current other mental health problem, any global or specific learning difficulty, such as dyslexia or dyscalculia that would prevent them from engaging easily with the online task materials. In line with health guidelines advocated by the 5:2 diet proponents and medical professionals, pregnancy, diabetes or any other medical condition for whom IF would potentially endanger participants' health, were also excluded. Participants were asked specifically about each of these criteria during an initial screening phone or Skype call.

To incentivise participation and discourage attrition, participants were entered into two prize draws to win multiple Amazon vouchers worth between £20 and £100; initially upon successful completion of the first part of the study, and lastly upon completion of the entire study.

Power calculation

As the study used a number of novel tasks with a new population, it was not possible to anticipate exactly what the effect sizes may be. However, a power analysis was informed by looking at the results reported for similar cognitive tasks in short-term fasting population using a similar repeated measures design (Bolton et al., 2014). Their results indicated a medium effect size could be expected when adults completed tasks in a full-fasted state. However, in our study participants would not be in a fully-fasted state as they would have ingested at least 250-300 calories prior to task completion. Therefore, it was estimated that a small effect size was more likely. A power calculation was carried out using G Power (Faul, Erdfelder, Lang, & Buchner, 2007). This gave an estimated sample size of 199 participants to provide 80% power with an alpha level of 0.05 for a dependent means matched-pairs design, to detect a small effect size (Cohen's dz = 0.2). Due to the joint nature of this project and anticipated attrition, researchers aimed to recruit enough participants to ensure sufficient power for both parts of the study.

Ethics

Ethical approval for this study (Project ID 6377/001) was sought from the UCL Research Ethics Committee. Approval was granted on 28th January 2015 for the duration of the project, until September 2016 (see Appendix IV for further details). Given that dieting is associated with the development of EDs, it was decided to target individuals who were already planning on pursuing this diet. Researchers were careful not to promote this diet or weight-loss in their advertising. It was decided to exclude participants who had any past/current history of an eating disorder from participation, given the levels of restriction involved in this diet. This eliminated the risk of triggering a relapse, in addition to the possibility of introducing bias. Given the common physical

side-effects of fasting, participants were advised to stop this diet immediately and seek medical advice, should they find themselves feeling unwell during the diet.

Study Design and Procedure

This was a joint study undertaken with another trainee, Jasmin Langdon-Daly, in which recruitment, overall procedural design and data collection were shared (please see Appendix III for further details). This study used a within-subjects, quasi-experimental design to compare neuropsychological performance on executive functioning tasks on fasting and non-fasting days during completion of the 5:2 diet.

Participants were asked to complete all online tasks at least twice (once on a fasting day and once on a non-fasting day), on days of their choosing during their third and fourth week of engaging in this diet. They could complete these measures twice more, on another fasting and non-fasting days should they wish; however, this was not mandatory in order to encourage retention. Participants were counter-balanced consecutively as they were recruited, so that half participants were instructed to complete their first testing session on a fasting day, and other other half on a non-fasting day, in order to address potential practice effects on tasks.

Participants were asked to complete these tasks in the evening between 6-10pm (due to potential time of day effects: Benau et al., 2014) in a quiet location, free of external distractions. They were asked to begin doing the tasks within 30 minutes of the initial starting time on each occasion, to ensure consistency across testing sessions. Due to the widely acknowledged impact of glucose levels on cognition (see Feldman & Barshi, 2007), participants were asked to eat something 30 minutes prior to doing these tasks on each occasion. On fasting days, they were asked to consume at least half of their calorie intake (250-300+ calories) by the time they completed the tasks, to ensure no participant was in a fully fasted state at the time of testing. Participants were asked to

list their food and drink intake up until the point of testing before each testing session, to highlight that the researchers were checking their calorie intake on fasting days, with the expectation that they would adhere to instructions. Self-reported motivation was assessed before completion of the tasks, and self-reported effort expended after. Task order was randomised for each participant on each testing session in order to reduce fatigue effects across tasks at a group level. Testing sessions lasted approximately 20 minutes. For further details regarding the appearance of the online platform used, please see Appendix X.

Interested individuals contacted the researchers by email. For details of all standard email correspondence, please refer to Appendix IX. They were then sent further information about the study and participation requirements, including inclusion and exclusion criteria (see Appendix VI for further details). Researchers then screened individuals for eligibility over the phone, where participants were also given the opportunity to ask any questions they required for informed consent. Following this, a participation schedule was co-constructed. Participants were given the study instructions verbally to ensure adequate comprehension, as completion of tasks took place remotely online. Participants were then asked to return a completed consent form (see Appendix VII), and provided with a written copy of the study instructions (see Appendix VIII) and the dates agreed for completion of tasks by email. They were asked to email the research team if they had decided not to complete the study to prevent unnecessary email prompts beyond this point.

At the beginning of their third week of dieting, participants were prompted by email to complete the two testing sessions online over the following two weeks. They were given a personal web address linked to their unique study ID number to complete these tasks. At the beginning of their fourth week, participants were sent another reminder email. Participants could contact the researchers by email at any point in the

study in order to address any issues that emerged during task completion to arrange further telephone/email support if needed. Comments could be left after each testing session to detect problems if they occurred or to submit qualitative feedback. Participants were only able to complete tasks on a computer, as opposed to a tablet or smart phone.

Pilot Study

A pilot study comprising of seven healthy adult volunteers (male and female, aged between 18-58) gathered through convenience sampling was carried out prior to recruitment. These volunteers were asked to complete the series of online tasks using different set-ups in their own homes (different operating systems - Mac, Windows or Linux; different internet browsers - Internet Explorer, Google Chrome, Safari) to ensure that they were able to complete the tasks remotely using instructions provided to them by the researcher. Qualitative feedback about the ease with which they completed the series of tasks was sought. This was used to adjust task administration and the number of trials presented in each testing session. Troubleshooting information was gleaned from this exercise and subsequently given to participants to reduce administration difficulties.

Measures

Demographic details. Participants were asked to provide information about their gender, age, country of domicile, native language spoke and highest educational attainment.

Body mass index (BMI). Participants' height and weight were self-reported in order to calculate their BMI score at the beginning of their diet, and again 4 weeks later.

BMI was calculated by dividing participants' weight in kilograms by their height in meters squared.

Motivation and effort. Intrinsic motivation to engage in the task was assessed by asking participants to complete a self-report visual analogue scale (VAS) online before each testing occasion. Participants used a sliding scale to indicate how motivated they felt to engage in testing. Participants were also asked how much effort they felt they put into each task using an additional self-report VAS after completion of tasks on each testing session.

Cognitive tasks. For further details regarding the online appearance and instructions provided for all tasks, please see Appendix X. For all cognitive tasks, participants were given the instructions on screen and an opportunity to practice the tasks to ensure sufficient comprehension before undertaking the real trials of each task. An accuracy threshold was set for some tasks during the practice trial, which was set at a level above that of chance. If participants didn't achieve this, they were requested to retake the practice trial again before proceeding. Participants gave their responses to tasks on screen, by tapping specific keys on the keyboard and using their mouse. Centered at the top of the screen a progress bar was displayed, indicating how far along in the completion of the test battery participants were during each task. Participants were asked to complete five tasks in total to measure various aspects of executive functioning: Tapping, Information Sampling, Trail Making Test - Part A&B, Rule Change Task and a 2N-back task with an embedded delayed intention task.

Psychomotor speed. A simple tapping task was was used to measure psychomotor speed as two studies have found slower completion times in healthy

acutely fasted adults during a two-finger tapping task (Green, Elliman, & Rogers, 1995, 1997). Computerised finger tapping tasks have been shown to moderate test-retest reliability (r = 0.74-0.79; Gualtieri & Johnson, 2006). Participants were asked to complete two consecutive trials, each lasting 15 seconds, where they were asked to press the space bar as many times as they could during each period while a countdown flashed on screen. The number of taps per trial was used as the outcome measure for this task.

Trail Making Test (TMT) is a widely used measure of neuropsychological performance across a number of cognitive domains, and is considered to be sensitive to neurological impairments in various populations with good psychometric properties, with alternative forms of reliability ranging from 0.78 to 0.92 for pen and paper based versions (Bowie & Harvey, 2006). However, it is acknowledged that computerized versions do not perform exactly the same (Drapeau, Bastien-Toniazzo, Rous & Cartier, 2007). TMT-Part A (TMT A) is often used as a measure of psychomotor speed and was included in our battery. Again this task was adapted for online administration where participants were presented with two visual arrays of yellow circles, one of numbers and one of letters placed in random order. In each trial, they were asked to click on the numbers in order (1, 2, 3 etc.) or the letters in order (A, B, C etc.) as quickly as possible until completion. Circles turned green if this was the correct order, or flashed pink if they made a mistake (see Figure 1). The average time taken to complete both trials was used to measure performance.

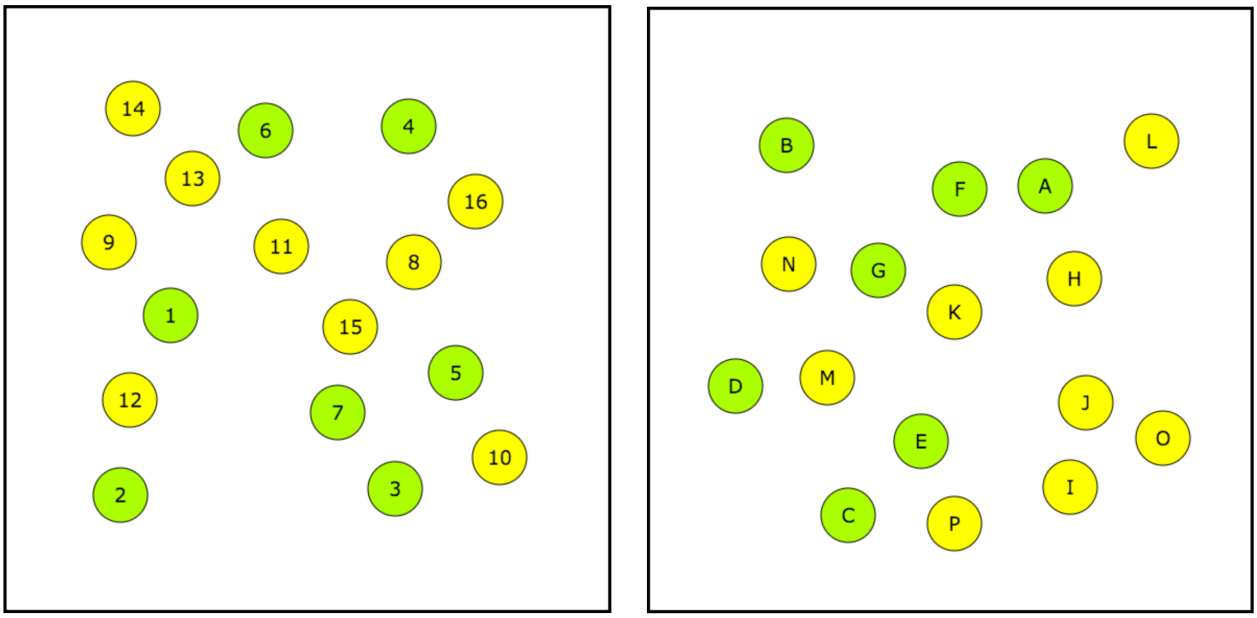

Figure 1 - Trail Making Test - Part A - Examples of numbers and letters trials

Set-shifting. Set-Shifting involves the ability to move or switch between different mental sets or tasks (Miyake et al., 2000). The first set-shifting task was an adaptation of a rule-change (RC) task that was first used by Bolton and colleagues (2014). In their study, they found that healthy female adults displayed significantly more set-shifting costs in an acutely fasted state than when satiated, in both food and nonfood (neutral) trials. Food trials use food items as stimuli to detect any potential food attentional biases that might be displayed during fasting states. Here, only neutral stimuli were used where participants were presented with a series of grey boxes on screen in a subitized manner (between one and six boxes in total, in a dice arrangement). They were asked to judge whether the number of boxes was high (four or more) or low (three or fewer), or whether there was an odd or even number of boxes, by asking the question: High?, Low?, Odd? or Even? (see Figure 2). On some consecutive trials the rule remained the same, a "stay trial" while on other trials, the rule changed, "shift trials". On each trail the probability of a change of task was one in three.

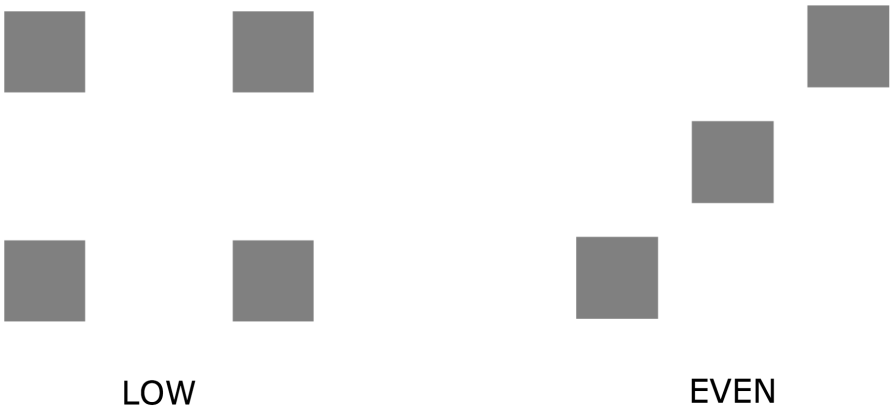

Figure 2 - Rule Change Task - examples of two different trials

Participants completed 100 trials during each testing session. Reaction time and accuracy were used to measure performance.

Part B of the TMT (TMT B) is often used to measure mental flexibility, as it requires participants to alternate between different mental sets. Use of TMT B was suggested by the eating disorder literature, as a meta-analysis carried out by Roberts, Tchanturia, Stahl, Southgate, and Treasure (2007) found that performance on TMT B in groups with AN and BN was impaired regardless of the state of their illness, though the pooled effect size was small (0.36). Research has suggested that TMT B performance measures set-shifting cost, with performance on this task correlating with another previously established experimental set-shifting task (Arbuthnott & Frank, 2000), suggesting concurrent validity. TMT B was adapted for online administration, and administered subsequent to part A. In this task, participants were presented with a visual array of numbers and letters printed in yellow circles on screen and presented in random order (see Figure 3). They were instructed to click on numbers and letters using their mouse/keypad in alternating order until completion (1, A, 2 B, 3, C etc.) as quickly as possible. Circles turned green if this was the correct order, or flashed pink if they made a mistake. Participants completed two trials of this task; however, the placement of the

visual arrange was randomised and changed each time. Average time taken to complete this task was used as the measure of outcome.

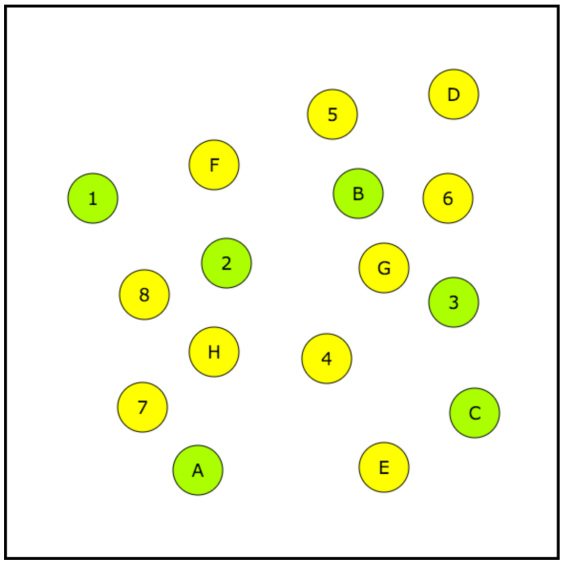

Figure 3 - Trail Making Test - Part B

Working memory. A 2n-back task was used to measure working memory, as it required participants to mentally manipulate information over a short period of time (Baddeley, 2003). Various n-back tasks have been used in previous eating disorder research paradigms, with one study finding that the number of errors in a 2n-back task was positively correlated to illness duration in an AN group (Dickson et al., 2008). While n-back tasks have been shown to be sensitive to differences in performance between adults with Parkinson's Disease and healthy controls; there is debate about whether these tasks are pure measures of working memory with studies failing to find convergent validity with well-established clinical measures of working memory (Miller, Price, Okun, Montijo, & Bowers, 2009). In this study, a 2n-back task was used similar to that used in Gilbert (2011). This was combined with an embedded prospective memory task similar to that reported in Gilbert (2015). Participants were presented with a series of neutral stimuli, single letters. Letters remained on screen until participants

made a response indicating whether the letter presented was the same as the letter presented two before over five minutes and 10 seconds, by pressing one key for "yes", and another key for "no". After responses, the screen remained blank for 250 milliseconds. Outcome measures used for this task were accuracy (average number of correct hits) and average reaction time.

Prospective memory. Prospective memory is the act of remembering to act upon a future intention, and has recently received more attention in research looking at the impact of nutrition on cognition (e.g. Riby, Law, Mclaughlin, & Murray, 2011), as it very clearly relates to real world demands, such as remembering appointments or taking medication. This task was embedded within the 2n-back task, as in the manner described by Gilbert (2011), but was temporally-related, as opposed to event-related. This task required participants to remember to do an additional action throughout the entire duration of the set-shifting task without any prompts being given, thus increasing the cognitive load. Participants were asked to press an additional key every 30 seconds for the duration of the task (within +/- 3 seconds) while performing the n-back task. They were able to press another key to display a clock briefly in the corner of the screen as many times as they wanted to help them maintain accuracy of response; however, this clock only remained visible on screen for 1.5 seconds. Performance was measured by measuring the number of times participants pressed the key within the right time (maximum of ten times), as well as the number of times they checked the clock.

Reflective impulsivity. An information sampling (IS) task was used to measure reflective impulsivity, defined as the process of collecting and analysing information before making a decision. This IS task measured the level to which participants sampled information before decision making occurred (Clark, Robbins, Ersche, & Sahakian,

2006), while ensuring demands on visual processing and working memory were minimised (delivered in a slightly modified format in this study). Previous research has demonstrated that in an acutely fasted state, participants opened more boxes in a matrix before making a decision about how many boxes were of a particular colour, than when satiated; but only in the fixed win condition where participants won 100 points, as opposed to the decreasing win condition where participants win 10 less points for every box opened (Howard, 2015). Therefore, only the fixed win condition was used in this study, so participants were not penalised for opening as many boxes as they wished. Participants were shown a visual array of twenty-five grey boxes, each of which could be uncovered by clicking on it to reveal a blue or yellow square, organised in a 5x5 matrix (see Figure 4). They were then asked to judge whether there were more blue or yellow squares overall, and could open as many boxes as they liked to inform their decision before making it. Once opened, boxes remained open for the duration of the trial to reduce working memory demands. Participants completed ten trials per testing session. Outcome measures extracted included accuracy (number of trials where the correct colour was chosen), amount of information sampled (total boxes opened), reaction time (each box) and overall duration of task (time taken for completion).

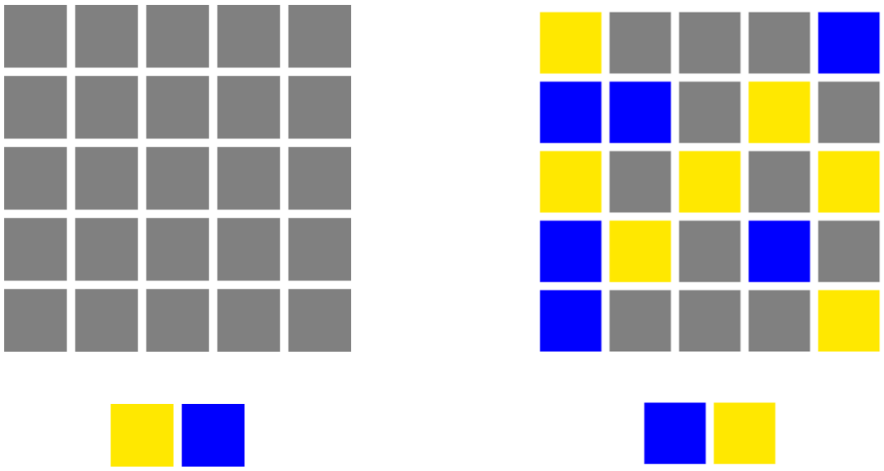

Figure 4 - Information Sampling Task - Examples of initial matrix and completed trial

Data Analysis

Prior to the analysis taking place, the data was screened carefully to exclude any data resulting from potential administration errors or failure to properly engage in the tasks, such as random responding or lack of comprehension, as this data was collected remotely in an uncontrolled environment. This involved the researcher inspecting each variable to detect if responses were at least more accurate than chance responding, and determining the time difference between the completion of each trial to ensure trials were completed within 90 minutes of the initial start time of day. Datasets were imported into Microsoft Excel initially, prior to the analysis taking place using IBM SPSS Statistics V22.0. Outliers were dealt with on a pairwise basis in each analysis by trimming each variable by creating an additional variable for each outcome measure in the SPSS file that specified whether or not a data point was considered an outlier. This resulted in different numbers being included in each analysis. A conservative approach to dealing with outliers was used, where data points were excluded if they exceeded 2.5 standard deviations (SD) from the mean within each analysis.

A series of mixed analyses of variance (ANOVA) was used to investigate our hypotheses to determine whether there was a difference in healthy adults' cognitive performance on fasting versus non-fasting days, while engaging in the 5:2 diet. In all analyses, the fasting order was entered as a between-subjects variable (i.e. those who initially completing tasks while fasted versus those who completed tasks first while non-fasted) to ascertain if it had any influence on test performance, while the fasting state (fasting day or non-fasting day) was entered as a within-subjects variable. Some trimmed variables did violate the assumption of normality; however, given that in all analyses the sample sizes were above 30, it was decided to proceed with parametric statistics (Norman, 2010; Pallant, 2013). On two occasions, the variables under scrutiny violated the assumption of homogeneity of variances; however, given that the numbers in each group were similar it was decided to proceed as there were no non-parametric alternatives (Pallant, 2013). Homogeneity of inter-correlations using Box's M statistic was also ensured prior to interpreting the test results.

Results

Participant Characteristics

Due to attrition from the study entirely or failure to complete all elements of the study, the number of participants eligible for analyses dropped throughout the study period from the initial number recruited (n = 177). 102 participants completed the first cognitive testing session but only 84 of those completed the second round, allowing their data to be considered for analysis. Due to the potential influence of the time of day on cognitive performance, 10 participants were excluded from the analyses as they failed to complete the second testing sessions within 90 minutes of the initial session, which was set as the cut-off point. However, the majority of the included sample (n =

74), completed the tasks within 30 minutes of the starting time of the initial testing session (n = 48: 65%). Only 14 participants completed four testing sessions (two fasting sessions & 2 non-fasting sessions), therefore there were insufficient numbers to conduct further statistical analyses on these data due to lack of statistical power. Hence, only data from the first fasting and non-fasting testing days were included.

The mean age of participants included in the analyses was 45.28 years (SD = 10.61, range = 23-65), and the majority of participants were female (n = 61, 82%). This was a highly educated sample, with most participants holding primary degrees (n = 27, 36%) or postgraduate qualifications (n = 31, 42%). Most participants resided in the UK (n = 52, 70%), but four continents were represented in the sample; most of whom would be considered developed/Western cultures (see Figure 5). Nearly all participants were native English speakers (n = 92%), regardless of their country of domicile, but all were fluent. No data on ethnicity was gathered. For further details, see Table 1.

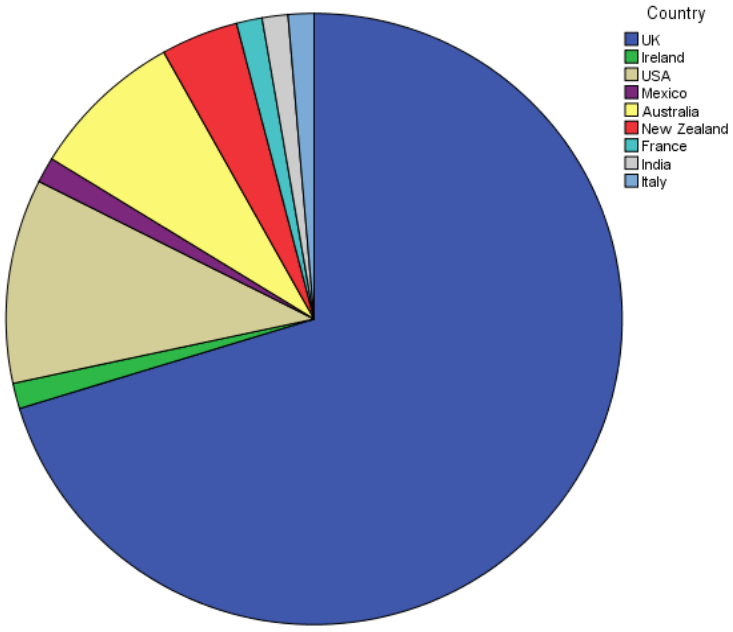

Figure 5 - Participants' country of domicile

The mean BMI of participants at the beginning of the study was 27.03 (SD = 4.94, range = 19.80 - 41.46), while after four weeks of being on the diet it was 26.23 (SD = 4.72, range 19.89 - 40.65). This difference was found to be highly significant using a paired samples t-test ($t(65) = 4.209$, $p < 0.001$), but the effect size was small ($r = 0.21$). This indicates that there was slight weight-loss overall at study completion; though closer inspection of the data reveals that the degree and direction of weight changes varied widely from individual to individual. All participants' BMIs fell above the 17.5 kg/m2 clinical cut-off for AN (WHO, 1992) at both time points; with inspection of box-plots revealing that most participants fell within the healthy to overweight ranges (BMI = 18.5 - 29.9) at both the beginning and end of the study, according to standard BMI weight status categories.

There were similar numbers of participants who completed their first testing session in a fasting state (n = 40, 54%) and in a non-fasting state (n = 34, 46%), indicating that the sample was reasonably counter-balanced to reduce the influence of any practice effects of tasks in our sample.

Table 1

Descriptive Statistics of Sample (n = 74)

Gender	61 Female	13 Male	
Age	Mean = 45.28 yrs	SD = 10.61 yrs	Range = 23 - 65 yrs
BMI Start	Mean = 27.43	SD = 4.93	Range = 19.80 - 41.46
BMI End	Mean = 26.57	SD = 4.84	Range = 19.89 - 40.65
Country of Domicile	52: UK	8: USA 6: Australia 3: New Zealand	1: Ireland, India, Italy, France, Mexico
Educational Level	31: Postgraduate qualification	27: Primary Degree	6: Secondary school 4: Doctoral level

Time Difference between Start Times of Testing Sessions	65% within 30 mins	20% within 60 mins	15% within 90 mins

Self-reported Motivation and Effort

There were significant positive correlations between self-reported motivation to engage and effort put into tasks, which were stronger in fasting ($n = 71$, $r = 0.485$, $p < 0.001$) than non-fasting states ($n = 69$, $r = 0.254$, $p = 0.035$), but the difference between these correlations was not significant ($z = 1.56$, $p = 0.118$). One way mixed between-within subjects' ANOVA was conducted to assess the impact of fasting order on participants' performance on self-reported motivation and effort expended using VAS measures on fasting and non-fasting days, where higher scores indicated increased motivation or effort. There was no significant interaction effect between fasting order and fasting state, for motivation: Wilks Lambda = 0.989, $F(1, 72) = 0.787$, $p = 0.378$, $\eta 2p = 0.011$ or effort: Wilks Lambda = 0.993, $F(1, 66) = 0.438$, $p = 0.511$, $\eta 2p = 0.007$. There were also no significant main effects for fasting state on either motivation: Wilks Lambda = 0.994, $F(1, 72) = 0.417$, $p = 0.521$, $\eta 2p = 0.006$ or effort: Wilks Lambda = 1.00, $F(1, 66) = 0.025$, $p = 0.876$, $\eta 2p < 0.001$), suggesting that participants felt similar levels of motivation and effort on fasting and non-fasting days. When looking at the effect of completing the tasks on a fasting day or non-fasting day first, again this did not to influence performance as there were no significant differences found, (motivation: $F(1, 72) = 1.123$, $p = 0.293$, $\eta 2p = 0.015$; effort: $F(1, 66) = 3.705$, $p = 0.059$, $\eta 2p = 0.053$). For information regarding descriptive statistics for the variables under discussion here, see Table 2.

Table 2

Descriptive Statistics for Self-reported motivation and effort

	Fasting Order	**Mean**	**SD**	**N**
Motivation -Fasting	*Non-Fasting First*	72.35	27.03	34
	Fasting First	70.30	25.60	40
	Total	**71.24**	**26.11**	**74**
Motivation - Non-fasting	*Non-Fasting First*	73.17	24.31	34
	Fasting First	65.07	23.92	40
	Total	**68.79**	**24.28**	**74**
Effort - Fasting	*Non-Fasting First*	85.00	12.79	31
	Fasting First	80.70	16.08	37
	Total	**82.66**	**14.72**	**68**
Effort - Non-fasting	*Non-Fasting First*	86.03	10.97	31
	Fasting First	79.02	17.22	37
	Total	**82.22**	**15.02**	**68**

Executive Functioning

Analyses revealed no significant differences between fasting and non-fasting performance on any executive functioning task used in this study. These analyses will be discussed in further detail below. For those analyses where interaction effects between fasting state and fasting order were observed, this indicates that there was a practice effects on those tasks, with performance improving from the first to the second testing session. However, given that fasting order was adequately counterbalanced in our sample with similar numbers of participants completing the tasks first while fasted

to those completing them first in a non-fasting state, these interaction effects will not be discussed further.

Psychomotor speed. As with the other cognitive domains, psychomotor speed performance was assessed using one-way mixed ANOVAs. Firstly, participants' performance on TMT A was examined, where task completion time (milliseconds) was the dependent variable. There was no significant interaction effect between fasting order and fasting state, Wilks Lambda = 1.00, $F(1, 71) = 0.009$, $p = 0.921$, $\eta 2p < 0.001$. There was also no significant main effect for fasting state, Wilks Lambda = 0.991, $F(1, 70) = 0.623$, $p = 0.432$, $\eta 2p = 0.009$ or fasting order , $F(1, 71) = 0.311$, $p = 0.579$, $\eta 2p = 0.004$, suggesting that performance was similar on fasting and non-fasting days, and that the order in which the initial tasks were completed had no significant bearing on performance.

A two-way mixed ANOVA was used to investigate participants' performance on the tapping task, where the first and second trial on the tapping task was entered as an additional within-subjects' independent variable to determine if there was a change in performance across each trial (e.g. fatigue effects), with the dependent variable being the number of taps completed within fifteen seconds. There were no significant interaction effects between any variables (see Table 3 for further details). There was no significant main effect for fasting state, Wilks Lambda = 0.999, $F(1, 68) = 0.091$, $p = 0.763$, $\eta 2p = 0.001$. There also was no significant difference in performance between those participants that completed their tasks first on a fasting day and those that completed their tasks first on a non-fasting day, $F(1, 68) = 3.104$, $p = 0.083$, $\eta 2p = 0.044$. However, there was a significant deterioration in performance between the first and the second tapping trials of moderate effect size, Wilks Lambda = 0.895, $F(1, 68) = 7.9393$, $p = 0.006$, $\eta 2p = 0.105$, suggesting that participants may have either become

fatigued or less motivated after completing the first trial. Please see Table 4 for information regarding descriptive statistics for the variables under discussion here.

In order to investigate the relationship between the psychomotor speed tasks used in this study, correlational analyses were carried out between tapping speed trials and TMT A using Pearson product-moment correlations. There were no significant relationships found between the number of taps on both trials and completion time on TMT A in either fasting or non-fasting states. Please see Appendix XI for the correlational matrix.

Table 3

ANOVA Table for Tapping Speed

	Wilks Lambda	**df**	**F**	**η2p**	**p**
Fasting State x Fasting Order	0.947	1, 68	3.801	0.053	0.055
Trial x Fasting Order	0.959	1, 68	2.936	0.041	0.091
Fasting State x Trial	1.000	1, 68	0.00	0.001	0.986
Fasting State x Fasting Order x Trial	0.961	1, 68	2.765	0.037	0.101

Table 4

Descriptive Statistics for Psychomotor Speed Tasks

	Fasting Order	**Mean**	**SD**	**N**
TMT A Mean Latency - Fasting	*Non-Fasting First*	19.42s	5.06s	34
	Fasting First	18.93s	3.89s	39
	Total	**19.16s**	**4.45s**	**73**
TMT A Mean Latency - Non-fasting	*Non-Fasting First*	19.79s	4.67s	34
	Fasting First	19.23s	3.49s	39
	Total	**19.49s**	**4.06s**	**73**

Tap Speed 1 - Fasting	*Non-Fasting First*	99.52	11.94	33
	Fasting First	91.62	12.88	37
	Total	**95.34**	**12.98**	**70**
Tap Speed 2 - Fasting	*Non-Fasting First*	95.97	11.97	33
	Fasting First	91.70	11.58	37
	Total	**93.71**	**11.87**	**70**
Tap Speed 1 - Non-fasting	*Non-Fasting First*	97.58	12.309	33
	Fasting First	93.97	11.50	37
	Total	**95.67**	**11.93**	**70**
Tap Speed 2 - Non-fasting	*Non-Fasting First*	95.58	12.01	33
	Fasting First	92.54	11.46	37
	Total	**93.97**	**11.74**	**70**

Set-shifting. A one way mixed between-within subjects ANOVA was conducted to investigate participants' performance on the alternating version of TMT (TMT B), where task completion time (milliseconds) was the dependent variable. There was a significant interaction effect between fasting order and fasting state, Wilks Lambda = 0.911, $F(1, 70) = 6.851$, $p = 0.011$, of moderate effect size, $\eta 2p = 0.089$. However, there was no significant main effect for fasting state, Wilks Lambda = 0.991, $F(1, 70) = 0.623$, $p = 0.432$, $\eta 2p = 0.009$, indicating that participants completed these alternating trials within similar times on fasting and non-fasting days. The difference between completion of the tasks on a fasting or a non-fasting day first was not independently significant, $F(1, 70) = 0.323$, $p = 0.572$, $\eta 2p = 0.005$.

In order to understand how fasting affected performance in the RC task, a two way mixed between-within ANOVA was carried out, where switch and stay trials were entered as an additional within-subjects independent variable, and the dependent variables were the number of correct responses (accuracy) and reaction time. There

were no significant interaction effects between any variables on accuracy (see Table 5 for further details). However, there was one significant interaction effect between fasting state and fasting order on reaction time. There was no significant main effect of fasting state for both accuracy, Wilks Lambda = 0.963, $F(1, 68) = 2.598$, $p = 0.112$, $\eta 2p = 0.037$, and reaction time, Wilks Lambda = 0.996, $F(1, 70) = 0.303$, $p = 0.584$, $\eta 2p = 0.004$. There were also no significant differences between the accuracy of those who initially performed tasks when fasting first versus those initially completing on non-fasting days (accuracy: $F (1, 68) = 1.150$, $p = 0.287$). There were significant reaction time differences with regard to fasting order: $F (1, 70) = 6.842$, $p = 0.011$, of moderate effect size ($\eta 2p = 0.089$), with participants who initially completed the tasks in a non-fasting state reacting more quickly than those who completed the tasks first while fasting.

As would be expected, trials including additional cognitive switching were more difficult than those without with highly significant differences between participants' performances on switch versus stay trials, for both accuracy, Wilks Lambda = 0.836, $F(1, 68) = 13.354$, $p = 0.001$ and reaction time, Wilks Lambda = 0.147, $F(1, 70) = 403.319$, $p < 0.001$. The effect size was small for accuracy ($\eta 2p = 0.022$), but large for reaction time ($\eta 2p = 0.853$). For information regarding descriptive statistics for the variables under discussion here, please see Table 6.

In order to investigate the relationship between the set-shifting tasks used in this study, correlational analyses were carried out to compare the set-shifting costs in TMT B (TMT B – TMT A) and the RC task (RC Shift – RC Stay) using parametric statistics. There were no significant relationships found between set-shifting cost measures on the TMT and the RC tasks, either with regard to RC reaction time or accuracy measures in either fasting or non-fasting states. Please see Appendix XI for the correlational matrix.

Table 5

ANOVA Table for Rule Change Task

Accuracy	**Wilks Lambda**	**df**	**F**	**η2p**	**p**
Fasting State x Fasting Order	0.978	1, 68	1.520	0.002	0.0222
Switch/Stay x Fasting Order	0.961	1, 68	2.755	0.039	0.102
Fasting State x Switch/Stay	0.978	1, 68	1.560	0.022	0.216
Fasting State x Fasting Order x Switch/Stay	0.995	1, 68	0.312	0.005	0.578
Reaction Time	**Wilks Lambda**	**df**	**F**	**η2p**	**p**
Fasting State x Fasting Order	0.539	1, 70	59.83	0.461	**<0.001**
Switch/Stay x Fasting Order	0.995	1, 70	0.335	0.005	0.564
Fasting State x Switch/Stay	0.991	1, 70	0.065	0.001	0.793
Fasting State x Fasting Order x Switch/Stay	0.954	1, 70	3.414	0.046	0.069

Table 6

Descriptive Statistics for Set-Shifting Tasks

	Fasting Order	**Mean**	**SD**	**N**
TMT - B Fasting	*Non-Fasting First*	23.16s	5.81s	34
	Fasting First	25.22s	6.22s	38
	Total	**24.25**	**6.08s**	**72**
TMT - B Non-Fasting	*Non-Fasting First*	24.13s	5.57s	34
	Fasting First	23.42s	4.32s	38
	Total	**23.76s**	**4.93s**	**72**
RC % Correct Switch - Fasting	*Non-Fasting First*	96.00	3.93	31
	Fasting First	93.48	5.77	39
	Total	**94.59**	**5.16**	**70**
RC % Correct Stay - Fasting	*Non-Fasting First*	96.29	4.50	31
	Fasting First	95.72	3.78	39
	Total	**95.97**	**4.09**	**70**

RC % Correct Switch - Non-fasting	*Non-Fasting First*	93.82	4.98	31
	Fasting First	93.03	5.91	39
	Total	**93.38**	**5.50**	**70**
RC Correct Stay - Non-Fasting	*Non-Fasting First*	95.39	4.17	31
	Fasting First	95.76	4.12	39
	Total	**95.59**	**4.12**	**70**
RC Switch RT - Fasting	*Non-Fasting First*	1387.16ms	210.99ms	33
	Fasting First	1624.54ms	226.29ms	39
	Total	**1515.74ms**	**248.31ms**	**72**
RC Stay RT - Fasting	*Non-Fasting First*	1101.61ms	162.14ms	33
	Fasting First	1325.01ms	144.12ms	39
	Total	**1222.62ms**	**188.49ms**	**72**
RC Switch RT – Non-Fasting	*Non-Fasting First*	1537.79ms	223.36ms	33
	Fasting First	1495.98ms	223.29ms	39
	Total	**1515.15ms**	**222.73ms**	**72**
RC Stay RT - Non-fasting	*Non-Fasting First*	1216.92ms	180.46ms	33
	Fasting First	1222.96ms	194.26ms	39
	Total	**1220.19ms**	**186.78ms**	**72**

Working memory. One way mixed subjects ANOVAs were carried out to investigate performance on the 2n-back task, using two dependent variables, accuracy (number of correct trials) and reaction time. For both accuracy, Wilks Lambda = 0.998, $F(1, 70) = 0.134$, $p = 0.715$, $\eta 2p = 0.002$, and reaction time, Wilks Lambda = 0.992, $F(1, 69) = 0.548$, $p = 0.462$, $\eta 2p = 0.008$, there were no significant main effects for fasting state. For both there were significant interaction effects between fasting state and fasting order (accuracy: Wilks Lambda = 0.876, $F(1, 70) = 9.93$, $p = 0.002$, $\eta 2p = 0.124$ and reaction time: Wilks Lambda = 0.678, $F(1, 69) = 32.75$, $p < 0.001$, $\eta 2p = 0.332$).

When looking the effect of completing the tasks on a fasting day or non-fasting day first on their own, again this did not seem to influence performance independently

as there was no significant difference found for accuracy, F(1, 70) = 0.082, p = 0.775, η2p = 0.001 or reaction time, F(1, 69) = 0.083, p = 0.774, η2p = 0.001. For information regarding descriptive statistics for the variables under discussion here, please see Table 7.

Table 7

Descriptive Statistics for Working Memory Tasks

	Fasting Order	**Mean**	**SD**	**N**
2N back - Mean Correct - Fasting	*Non-Fasting First*	87.22	7.93	34
	Fasting First	84.50	7.02	38
	Total	**85.79**	**7.53**	**72**
2N back - Mean Correct - Non-fasting	*Non-Fasting First*	85.22	7.21	34
	Fasting First	87.03	7.48	38
	Total	**86.18**	**7.36**	**72**
2N back - Reaction Time - Fasting	*Non-Fasting First*	965.64ms	191.83ms	33
	Fasting First	1088.15ms	225.51ms	38
	Total	**1031.21ms**	**217.92ms**	**71**
2N back - Reaction Time - Non-Fasting	*Non-Fasting First*	1060.87ms	199.23ms	33
	Fasting First	964.63ms	207.90ms	38
	Total	**1009.36ms**	**208.15ms**	**71**

Prospective memory. Participants' ability to complete a task over a forthcoming period of time, specifically their ability to remember to check the timing on the clock (remembering) and accuracy of hits within instructed timeframe (accuracy), was investigated using one way mixed ANOVAs. There was no significant interaction effect between fasting order and fasting state, for both remembering: Wilks Lambda = 0.995, F(1, 60) = 0.314, p = 0.577, η2p = 0.005, and accuracy: Wilks Lambda = 0.960, F(1, 67) = 1.732, p = 0.577, η2p = 0.005. There were no significant main effects for

fasting state on both remembering: Wilks Lambda = 1.000, F(1, 60) = 0.023, p = 0.881, η2p > 0.001, and accuracy outcomes: Wilks Lambda = 0.975, F(1, 67) = 1.732, p = 0.193, η2p = 0.025. The same was also true for fasting order, as there were no significant differences between groups that completed tasks first while fasted compared to those completing them first in a non-fasted state, with regard to both remembering, F(1, 60) = 3.406, p = 0.020, η2p = 0.054 and accuracy F(1, 67) = 0.617, p = 0.435, η2p = 0.009. For information regarding descriptive statistics for the variables under discussion here, please see Table 8.

Table 8

Descriptive Statistics for Prospective Memory Tasks

	Fasting Order	**Mean**	**SD**	**N**
Number of Clock Checks - Fasting	*Non-Fasting First*	17.86	7.68	28
	Fasting First	22.03	8.91	34
	Total	**20.15**	**8.57**	**62**
Number of Clock Checks - Non-Fasting	*Non-Fasting First*	18.57	9.16	28
	Fasting First	21.62	8.56	34
	Total	**20.24**	**8.90**	**62**
Correct Clock Hits - Fasting	*Non-Fasting First*	8.30	1.55	30
	Fasting First	7.51	1.86	39
	Total	**7.86**	**1.76**	**69**
Correct Clock Hits - Non-Fasting	*Non-Fasting First*	7.43	1.97	30
	Fasting First	7.62	2.36	39
	Total	**7.54**	**2.19**	**69**

Reflective impulsivity. Aspects of participants' performance on the information sampling task were investigated using one way mixed ANOVAs, looking at their accuracy (number of correct trials), degree of information sampling prior to decision

making (mean number of boxes opened per trial), mean latency per box (average amount of time elapsed before opening another box) and speed (mean trial completion time). There were no significant main effects for fasting state on any outcome measure (accuracy: Wilks Lambda = 0.992, F(1, 72) = 0.548, p = 0.462, η2p = 0.008; information sampling: Wilks Lambda = 0.997, F(1, 72) = 0.182, p = 0.671, η2p = 0.003; mean latency: Wilks Lambda = 0.984, F(1, 69) = 1.111, p = 0.295, η2p = 0.016, and speed: Wilks Lambda = 0.992, F(1, 69) = 0.575, p = 0.451, η2p = 0.008). Fasting order did not distinguish between group performance independently as participants performed similarly across all outcome measures (accuracy: F(1, 72) = 0.295, p = 0.589, η2p = 0.004; information sampling: F(1, 72) = 3.903, p = 0.052, η2p = 0.051; mean latency: F(1, 69) = 0.233, p = 0.638, η2p = 0.003, and speed: F(1, 69) = 1.186, p = 0.280, η2p = 0.017).

There were no significant interaction effects between fasting state and fasting order on participants' degree of accuracy (Wilks Lambda = 0.982, F(1, 72) = 1.299, p = 0.258, η2p = 0.018) or information sampling (Wilks Lambda = 0.995, F(1, 72) = 0.333, p = 0.566, η2p = 0.005). However, there were highly significant interaction effects of moderate effect sizes between fasting state and fasting order noted with regard to aspects of time taken: mean latency per box (Wilks Lambda = 0.874, F(1, 69) = 9.965, p = 0.002, η2p = 0.126) and speed (Wilks Lambda = 0.876, F(1, 69) = 9.766, p = 0.003, η2p = 0.124). Please see Table 9 for information regarding the descriptive statistics for the variables under discussion here

Table 9

Descriptive Statistics for Reflective Impulsivity Tasks

	Fasting Order	**Mean**	**SD**	**N**
IS Correct Trials - Fasting	*Non-Fasting First*	8.26	1.28	34
	Fasting First	8.35	1.49	40
	Total	**8.31**	**1.39**	**74**
IS Correct Trials - Non-fasting	*Non-Fasting First*	8.61	1.18	34
	Fasting First	8.27	1.17	40
	Total	**8.43**	**1.18**	**74**
IS Mean Boxes Opened - Fasting	*Non-Fasting First*	15.51	5.30	34
	Fasting First	17.97	5.42	40
	Total	**16.84**	**5.47**	**74**
IS Mean Boxes Opened - Non-fasting	*Non-Fasting First*	15.88	4.51	34
	Fasting First	17.91	5.11	40
	Total	**16.98**	**4.92**	**74**
IS Mean latency per box - Fasting	*Non-Fasting First*	960.09ms	288.27ms	33
	Fasting First	1024.13ms	333.08ms	38
	Total	**994.37ms**	**312.51ms**	**71**
IS Mean latency per Box - Non-fasting	*Non-Fasting First*	1021.82ms	287.49ms	33
	Fasting First	900.50ms	210.86ms	38
	Total	**956.89ms**	**254.95ms**	**71**
IS Mean total time - Fasting	*Non-Fasting First*	13.74s	6.63s	33
	Fasting First	16.64s	5.71s	38
	Total	**15.29s**	**6.28s**	**71**
IS Mean total time - Non-fasting	*Non-Fasting First*	14.90s	5.66s	33
	Fasting First	14.74s	4.64s	38

	Total	**14.82**	**5.10s**	**71**

Overall Executive Functioning Reaction Time and Accuracy.

Finally, to examine the overall differences in performance between fasting and non-fasting performances across all tasks together, an overall composite variable was computed for both reaction times and accuracy across all executive functioning tasks.

This was done by summing computed z-scores for all reaction time related outcome measures [(-Tapping_1) + (-Tapping_2) + IS_Mean latency per box + IST_Mean total time + 2Nback_Reaction time + RC_Reaction time Switch + RC_Reaction time Stay + TMT A + TMT B], and all accuracy related outcome measures [IS_Number correct + 2Nback_Correct + PM_Correct hits + RC_Correct Switch + RC_Correct Stay] in both fasting and non-fasting states. The tapping trial measures were reverse scored as higher scores on this measure indicated greater ability, compared to the lower scores on all other reaction time measures. Wilcoxon signed-rank tests were then carried out to investigate the overall differences between reaction times and accuracy, across all the executive tasks as a whole using these composite measures. Results indicated that there were no significant differences on group performances between fasting and non-fasting days with regard to reaction times ($z = 1315$, $p = 0.696$) and accuracy ($z = 1367$, $p = 0.912$) across tasks (see Figure 6). Please see Table 10 for information regarding the descriptive statistics for the variables under discussion here

Table 10

Descriptive Statistics for Overall Reaction Time and Accuracy Composite Scores

	Mean	*Median*	*Mode*	*SD*	*N*
Overall Reaction Time - Fasting	0	-0.38	-11.56[a]	5.43	74
Overall Reaction Time - Non-fastin	0	0.05	-11.47[a]	5.39	74
Overall Accuracy - Fasting	0	0.52	-11.45[a]	2.98	74
Overall Accuracy – Non-fasting	0	0.51	-11.32	2.77	74

a. *Multiple modes exist. The smallest value is shown*

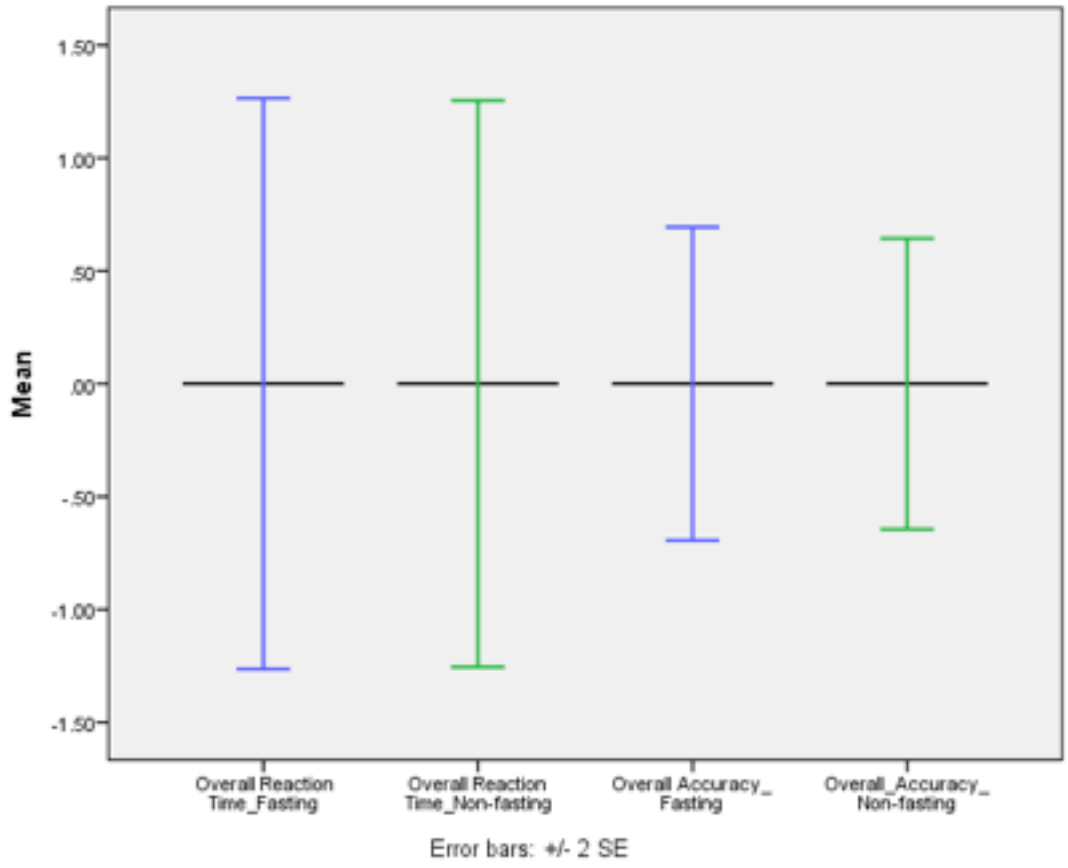

Figure 6 – Bar chart depicting the overall Z reaction time and accuracy composite EF scores in both fasting (blue) and non-fasting (green) states

Discussion

This study investigated the impact of the intermittent fasting on executive functioning in healthy adults, by comparing their performance on fasting and non-fasting days in their first month of doing the 5:2 diet. Unlike many previous studies, this study sought to understand the cognitive impact of a significant (approximately one quarter of recommended daily guidelines) but not absolute restriction of calorie intake in adults, who reported being healthy. A consistent pattern of performance emerged across all the cognitive tasks administered. Our results suggest that there was no significant impact, either positively or negatively, on adults' ability to perform tasks that looked at set-shifting, working memory, prospective memory, reflective impulsivity and psychomotor speed, as performances were similar across fasting and non-fasting days in our sample. However, given that this study may have been underpowered, there is not strong enough evidence to suggest yet that there are no detrimental cognitive effects for adults undertaking this diet in the short-term, when they are engaged in daily tasks that require executive skills. Participants also reported feeling similarly motivated to engage in testing, having also made similar levels of effort on fasting and non-fasting days.

Our initial hypothesis was not supported as there was no change in executive functioning performance on fasting and non-fasting days. The same pattern of executive functioning deficits that has been observed in individuals with eating disorder diagnoses was not observed in our healthy adult sample, which did not lend support to our second hypothesis. Our sample did not demonstrate impairments in executive functioning on fasting days when participants had ingested minimal calories. This may suggest that the executive functioning impairments observed in individuals with EDs are pre-morbid or related to the prolonged effects of calorie deprivation (i.e. a cognitive scar), and not resulting from the effects of insufficient calorie intake on any given day. There may be

alternative explanations for our findings, which will be discussed in detail below. For one of the set-shifting tasks, the RC task, there was a main effect for fasting order, with participants who initially completed the tasks in a non-fasting state reacting more quickly those that completed them first while fasting. However, given that fasting order was randomly allocated and counterbalanced in our sample, this is likely to be a false positive result.

As this study was the first of its kind with regard to examining the cognitive impact of intermittent fasting using the 5:2 diet, there are no directly comparable studies. However, our results deviate from findings reported in the literature about the impact of acute fasting states on adults' cognitive functioning. Bolton and colleagues (2014) did find in a similarly sized adult sample that after 16 hours, set-shifting performance on the RC task was impaired. Another study reported that when fasted for over 20 hours, adults' performance changed on the IF task, in that they opened more boxes, took longer and made fewer errors, indicating decreased reflective impulsivity. However this study only used young female participants (Howard et al., unpublished). Not all studies have found a complete fast (water only) to lead to cognitive changes. Using a very clever methodology, researchers used a double-blind, placebo-controlled trial to investigate the impact of a two day calorie deprivation on a group of healthy young adults (Lieberman et al., 2008). Their results indicated that the group, who unknowingly were fed non-nutritive food, demonstrated no cognitive impairments over the duration of the 48 hour nearly-full fast, on tasks that measured vigilance, choice reaction time, learning, memory, and reasoning. These tasks previously demonstrated sensitivity to various environmental changes. This well-controlled study also found relatively stable concentrations of glucose throughout the 48 hour period, suggesting that homeostatic mechanisms buffer changes in blood glucose during short periods of fasting.

Our results are in line with findings reported from studies investigating the cognitive impact of various calorie-reduced dieting methods aimed at weight-loss. A randomised control trial, CALERIE, run in the US sought to investigate the physical, psychological and cognitive impact of a continual 25% reduction in daily calorie intake on non-obese adults from 25-45 years old. In the initial phase of this trial, researchers compared baseline cognitive functioning comprising of aspects of verbal and visual memory and attention to functioning in the third and sixth month of dieting (Martin et al., 2007). Their results indicated no significant changes in performance across the testing sessions, leading them to conclude that this reduction in calorie intake did not affect cognitive functioning, especially as the degree of daily deficit was not associated with a change in cognitive performance. It must be noted that the sample size was small, with only twelve people in each treatment arm, suggesting that their study may have been underpowered. They did not examine executive functioning in their study. Other researchers compared the cognitive performance of overweight adult women, of similar mean age to our sample, before and after three months of engaging in a diet that was designed to reduce overall energy intake by 20%, to a healthy control group (Bryan & Tiggemann, 2001). Their well-designed study used alternate versions of tasks on each testing occasion examined processing speed, executive functioning (using TMT A&B), working memory, along with immediate and delayed recall and recognition memory. Their findings suggested little or no cognitive impact as a result of dieting. The only significant finding was that while dieting, participants showed more intrusions during a free recall memory task.

One of the main sources of comparison for intermittent fasting are studies that have investigated cognitive functioning during Ramadan, a yearly thirty-day period during which Muslims fast from sun up to sun down, without ingestion of food or fluids. Depending on the time of year and geographical location, participants may fast

for between 6 and 20 hours at a time. Many of these studies have been conducted with groups of young athletes; though many of the sample sizes are very small, leaving these studies vulnerable to being underpowered. One such study looked at the impact of time of day on aspects of cognitive functioning using computerised testing battery, including psychomotor speed, visual attention, visual and verbal learning and memory, and executive functioning in the morning and late afternoon on fasting days during Ramadan in young male athletes (Ho-Heng et al., 2011). They found different cognitive domains were affected differently at different times of the day, with improved attention and psychomotor speed in the morning while fasting, and a deterioration in verbal learning and memory performance in late afternoon, after they had been fasting for many hours. Like our study, they did not find any effect of fasting on working memory performance.

Taking the evidence base as a whole, including our findings, it seems that while absolute restriction of calorie intake for significant periods of time (16-24 hours) may lead to cognitive impairments in particular cognitive domains thought to be sensitive to calorie deficits (i.e. executive functioning), it may be that even minimal calories (up to 25% in our study) may protect against cognitive impairments in the short-term.

Alternative Explanations

There was a high attrition rate in our study (52.54%), with just under half of the initial participants completing the cognitive component of this study. However, a recent systematic review of commercial dieting for weight-loss programs in the US found attrition rates varied between 2.5% and 56% within the initial months or year of the diet (Tsai & Wadden, 2005). This suggests that the rate of attrition in our study may not that unusual when compared to other popular dieting strategies. However, it must be stated that we cannot cannot rule out that participants may have continued with the diet,

despite dropping out of the study. Among those participants who provided a reason for their drop-out, reasons cited included life events, illness and inability to carry out daily activities due to perceived negative impact of diet on their daily functioning. This could mean that participants in the final sample were those adults who were better able to tolerate the effects of a significant reduction in calorie intake, or that it had less of an impact on them.

One hypothesis could be that this may be due to differences in glucoregulation, the ability to control blood glucose levels, that is part of the body's natural homeostatic mechanism. Even when levels are within the normal range, these individual differences in glucoregulation have been associated with differences in cognitive functioning (Benton, Parker, & Donohoe, 1996). Glucose levels have been demonstrated to facilitate cognitive functioning, especially those tasks that are more cognitively demanding and under conditions of divided attention, with these effects being more pronounced in healthy older people (Philippou & Constantinou, 2014). In our study, we requested that participants eat something 30 minutes before completing cognitively demanding, executive tasks, in an attempt to bring greater consistency. It is known that calorie intake increases blood glucose levels, which one study has estimated in healthy adults to peak between 45-50 minutes (Freckmann et al., 2007). It is recognised that blood glucose levels are affected by a multitude of external factors that were not measured in our study. Given the online nature of data collection, it was not possible to measure blood glucose levels in our sample, but it would be useful for future studies to do this.

One could speculate that the adults who stuck with the diet in our study had better glucoregulation. Therefore, these results may only be applicable to a select group of adults, for whom there are no consistent negative cognitive effects for engaging in intermittent fasting. It is possible therefore that in testing other groups of adults who are

more sensitive to the effects of calorie restriction, subtle cognitive differences on fasting days may be seen while doing the 5:2 diet.

Strengths and Limitations

This study utilised a repeated measures design, allowing each participant to act as their own control. The advantage of advertising and collecting data online is that it allowed the recruitment of a sample of adults living in many countries worldwide. This makes the results of our study applicable to a wider group of people than just young adults in university, which is an often-used population in this area of research, and also indicates the popularity of this diet around the globe. Examining the cognitive functioning of healthy adults who have decided to engage in intermittent dieting in their daily lives also provides more ecological validity with regard to understanding the functioning individuals with EDs who regularly restrict their calorie intake, in comparison to absolute fasting. Individuals with EDs who restrict do not often totally restrict their calorie intake on a daily basis, instead ingesting minimal but insufficient calories on some days. This will vary according to the severity of their illness and whether or not they also binge.

Our participants were self-selecting, and as such this may have introduced some sampling bias due to positive response bias. Many reported at screening that they were very invested in the diet working. Some stated that they believed it may serve as a potential protective factor against cognitive decline in later life, as opposed to pursuing the diet purely for weight-loss reasons. As mentioned above, the high rate of attrition as the study progressed may further have contributed to sampling biases, leading to a sample that may have been better able to tolerate the effects of such a significant reduction in calorie intake on fasting days. With regard to design limitations, our data collection took place remotely online, leading to less controlled, and thus less consistent

environmental testing conditions. We were also reliant on participants' adhering to the set calorie restrictions on fasting days, without any means of checking their adherence, other than their written reports of food and fluid intake on the days of testing. Their reports may be prone to error due to social desirability bias or lack of accurate recall.

Due to the size of the final sample included in our analyses, our study was not sufficiently powered to detect any small sized differences in performance on these tasks from fasting to non-fasting days that were likely (if present), given that our participants had ingested some calories in the half hour just prior to task completion. While our initial sample recruited into the study approached the number required for sufficient power, the high rate of attrition, in addition to the need for exclusion of datasets to maintain accuracy, resulted in a much smaller sample. The final sample was only sufficiently powered to detect medium or large effect sizes. Therefore, while we have some evidence to suggest that there is no medium to large-sized differences in adults' cognitive performance from fasting to non-fasting days when engaged in the 5:2 diet, more research using a larger sample is required to investigate the presence of any small-sized differences in performance.

One further limitation of the study is the design of the prospective memory task used in this study. This task was embedded within another task, instructing the participant to remember to act in the future while performing another unrelated activity, meaning that the action required was not cued by the retrieval environment, and as such would meet criteria for a prospective memory task (Einstein & Smith, 1997, p. 487). However, the unit of temporal measurement (30 +/- 3 seconds) required for accurate task completion may be too short and too frequent to be considered an ecologically valid measure of prospective memory. Further research should incorporate a prospective memory task using a much longer temporal interval between the instruction and cue to

action, such as days or weeks for improved ecological validity, which may better relate to real-world prospective memory demands faced by potential 5:2 dieters.

Clinical Implications and Future Directions

This study is the first of its kind to investigate the cognitive functioning of individuals engaging in the 5:2 diet. Our results will allow potential dieters to be better informed about how this diet affects executive functioning, skills that are necessary for all aspects of daily life. Our results suggest that in the short-term, this style of intermittent fasting may not lead to any cognitive risks or benefits in healthy adults. This style of fasting may be an effective way of retaining cognitive functioning for some people, even when deprived of most of the recommended calorie intake on two days, as opposed to full fasting states. Future studies should aim to compare the cognitive functioning of healthy individuals engaged in the 5:2 diet with those on daily calorie restrictive diets over a longer period, to determine if there are any differences between these groups. Glucose levels should be measured before each testing session in order to better understand how the individual differences in glucoregulation effects performance during caloric restriction.

To suggest that the 5:2 diet is associated with no detrimental or positive cognitive impact is premature, as much more research needs to be conducted. Our research was conducted in the initial month of the diet, and what remains unknown is how this diet affects executive functioning in the longer term when the cumulative calorific deficit would be larger. Longitudinal research using intermittent fasting designs is more ecologically valid when considering the cognitive effects of prolonged calorie deprivation on individuals suffering from restricting EDs. Intermittent fasters are also deliberately restricting their calorie intake to minimal amounts on certain days on a

continual basis in environments where they are often surrounded by cues to eat which they have to resist, similar to people with EDs who restrict.

It is important to reflect on the wider implications of our study by considering the relationship of these findings to clinical work with individuals with EDs. Quantifying the degree to which the cognitive functioning of individuals with EDs is influenced by insufficient calorie intake would be useful. More information about this would aid clinical decision making about how best to structure eating disorder treatment programs. This might include the timing and focus of the various components of treatment, such as weight-restoration and therapy. If it is known when a person's cognitive functioning is least likely to be impacted by starvation, this would increase their capacity to engage in therapy. Further research incorporating incremental calorie intake designs may aid an understanding of the observed cognitive deficits in EDs and the inconsistencies in previous studies' results. This is needed given the delicate balance observed in animal studies between calorie intake and cognitive functioning. It may be that even minimal calorie intake serves to protect cognitive function in the short-term, due to the body's own homeostatic processes. This may explain why younger adults with AN are still able to maintain their cognitive functioning. Subtle deficits, if any, are observed in younger populations with AN (please refer to systematic review for further details). This pattern is different to the cognitive functioning of adults with AN, who often have much longer durations of illnesses.

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Part 3: The Critical Appraisal

Nutrition and Cognition:

Reflections on the Research Process

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"Eating disorders are of great interest to the public, of perplexity to researchers, and a challenge to clinicians."

Fairburn and Harrison (2003), p. 407

The quote from Fairburn and Harrison (2003), experts in the eating disorders (ED) field, sums up the various perspectives there are on EDs. My motivation to undertake this research came from experiences of encountering individuals with EDs in my clinical and voluntary work. Consequently, I have become aware of how the lives of those suffering from EDs and their carers/families can become all consumed with managing their condition. Sadly, for some individuals, EDs can become life-threatening.

EDs are associated with very high rates of morbidity and mortality, including high rates of suicide (Arcelus, Mitchell, Wales, & Nielsen, 2011), with anorexia nervosa (AN) presenting with the highest mortality rate of all mental health conditions (Agras, 2001). Though their incidence and prevalence in the general population is rarer than other mental health conditions, in certain groups, such as adolescent females, they are relatively common and may be on the rise (Smink, Van Hoeken, & Hoek, 2012). EDs are associated with very high economic costs and therefore, place a burden on society at large. Recent estimations by Beat, the eating disorders charity, suggest they may cost the UK approximately £15.5bn annually (Beat, 2015). Together, these statistics indicate that EDs present a significant societal problem, and one that warrants further research.

EDs present a puzzle, and one that is still far from being fully understood. They were first described in the medical literature in the 1680s by Dr. Richard Morton in London (Silverman, 1983). He was the first to give a medical account of AN, describing

his twenty-year old female patient, Miss Duke, as a "skeleton only clad with skin" in his book, a "Treatise of Consumptions" (Morton, 1694). He hypothesised that her sadness ate away at her until her death, thus linking her emotional and physical state. This inextricable intersection between psychological and physical wellbeing is more evident in EDs, when compared to many other mental health difficulties, and heightens their complexity. As EDs progress, those bidirectional physical and psychological influences intensify the course of the illness, making recovery less likely the longer its duration (Treasure, Stein, & Maguire, 2015). In addition and contrary to many other psychological difficulties, EDs are often highly valued by the person concerned (Serpell, Treasure, Teasdale, & Sullivan, 1999), making them even more difficult to treat.

It may be initially challenging for readers outside of the field of EDs to understand the link between the presented systematic review and empirical papers of this thesis. How does research investigating the impact of an intermittent fasting diet on cognition in healthy adults relate to the neuropsychological profile of adolescents with AN? Given the inherent difficulties in disentangling the effects of starvation from the pre-morbid neuropsychological risk factors in EDs populations, there is a need to use a wide array of methodologies when conducting research in these disorders. Research needs to look at how reductions in calorific intake affects neuropsychological/cognitive functioning in both healthy individuals, and in individuals with EDs, in order to fill in some of the missing pieces of this complex puzzle.

Systematic Review

"With an ever-increasing plethora of studies being published in the health sciences, it is challenging if not impossible for busy clinicians and researchers alike to keep up with the literature."

Uman (2011), p. 57

One of the key elements of the scientific method is that of replication. Without this vital step, it is impossible to know if the outcomes of research are merely that of chance, or represent an underlying pattern that is applicable to a wider group than one's initial sample. Systematic reviews of the evidence base provide the reader with a far better picture of the underlying patterns observed, than reading the results of one individual study. Textbooks quickly become outdated with regard to the neuropsychology of EDs, due the volume and speed of the publication of studies concerning this area in recent years. Therefore, systematic reviews are an ideal way of keeping busy clinicians updated on the current state of the evidence base. Clinicians can then use this information to inform their practice, and decide on better assessment protocols.

Motivation underpinning Systematic Review

My rationale for undertaking this particular review was influenced by my clinical work in a specialist child and adolescent ED service. I was struck there by the lack of clarity surrounding the degree to which the current neuropsychological functioning of a young person who is very unwell with AN is the cause or result of their condition and subsequent starvation. In severely underweight states, it was often considered useful to postpone individual therapy with young people with AN until some weight-gain was achieved. And yet these young people were often still performing well academically, continuing to achieve high grades in exams, despite being significantly

underweight. Better understanding about the effects of starvation would be clinically useful when formulating and delivering interventions in EDs. Given my experiences in paediatric neuropsychology, I was aware that it is unhelpful to assume that the neuropsychological outcomes in adults are going to be the same in growing children and adolescents. This is due to the differential impact that insults can have on a developing brain (Anderson, Northam, & Wrennall, 2014).

Need for a Developmental Approach

This review has demonstrated the need to contextualise the results of a study within the relevant body of literature. By examining the evidence base as a whole, is becomes apparent that the picture of neuropsychological functioning in children and adolescents with AN is far from clear. No consensus about a distinct profile in this younger group can be drawn yet, unlike in adults, where there is a more distinct profile. Even for those domains that have been cited as potential endophenotypes for EDs, such as poor set-shifting and weaker central coherence, the picture painted in this review was inconsistent. Many studies under review did not find any relative impairments in these domains. The lack of replication of the neuropsychological profile found in adults in younger populations casts doubt on the idea of a static neuropsychological profile in AN. Some researchers have proposed a neurodevelopment model for AN, using evidence from both clinical and basic science research (Connan, Campbell, Katzman, Lightman, & Treasure, 2003). This demonstrates the need to take a more developmental approach to determining the neuropsychology profile of AN.

Different neuropsychological functions develop at different rates, even within domains (Anderson et al., 2014). Executive functioning skills, such as those mentioned above, are typically some of the last to develop in childhood and adolescence, but even these skills develop at different rates, with attentional control maturing earlier in

childhood than cognitive flexibility (Anderson, 2002). One hypothesis for the lack of consistency between adolescent and adult findings could be that the picture in AN is one of emerging impairments, which may only be observable when the task demands exceed capacity, such as in late adolescence or adulthood. This could result from either pre-morbid neuropsychological patterns, or the sustained impact of calorific restriction on a developing brain, during a sensitive period for the development for specific cognitive domains. This review noted younger populations with AN, like adults, tend to display average to high average intellectual functioning across a range of measures. It may be that these usually subtle impairments when present, do not reveal themselves until the more difficult tasks are used, given their level of intellectual functioning. These more sensitive tests are often not typically developed for use with younger populations. Therefore, certain tasks may be insufficiently sensitive to detect subtle impairments due to ceiling effects, especially in high functioning populations.

The outcome of this review suggests the need to design a testing battery for use in research or clinical settings that has previously demonstrated sensitivity in the population concerned. It also raises the issue of developing standardised outcome measures that are fit for purpose and widely available for use, for both direct and indirect measures of neuropsychological functioning. One of the current difficulties in using neuropsychological measures in psychiatric populations in general is that these standardised and normed tasks were not designed for use with this group. Thus, there is a need for standardised tests to be developed for use in these populations, where gross impairments are less likely than in populations with neurological conditions.

Importance of Case Series

One of issues identified in conducting this systematic review is the difficulty of applying knowledge gained from cohort studies to working clinically with a single

individual. The diversity typically inherent in individuals' profiles is lost when analyses and the reporting of such analyses, takes place only at a group level. Therefore, this makes it difficult to determine how much variability is typical, as opposed to a cause for concern. Some of the case series in this review were conducted with the explicit aim of demonstrating variability as opposed to stability in patterns of functioning. These are equally important papers for clinicians to read as they keep the individual nature of the cognitive profile at the forefront. Selective case studies such as these remind clinicians that there may be more than one pattern evident in a particular population, and also that wide variation from the averaged group means may be entirely typical within this population.

Inconsistencies in Findings

Turning now to the lack of consistent findings reported in our review, this does not necessarily mean that there are no consistent patterns in the neuropsychological profile of adolescents with AN. This lack of consistency is more likely the result of the numerous influences on cognition present and the multitude of tasks used to measure the same domain in this population. Until it is possible to determine the relative influence of psychoactive medication, co-morbidities, age at onset, duration of illness and intake of calories on testing days on functioning in this population, inconsistent findings are likely to continue to be reported. Ways of measuring this influence include taking these potential confounds into account in the analyses and not excluding individuals with any of these factors from the sample. The presence of co-morbidities and psychoactive medication are common in individuals with AN. For example, one German study found that 73.3% of female adolescents with AN met criteria for at least one other co-morbid Axis I disorders using DSM-IV criteria, with mood and anxiety disorders being the most commonly diagnosed (Salbach-Andrae et. al., 2008).

Neuropsychological Assessment in Adolescents with AN in Clinical Settings

As stated previously, this review illustrates the lack of a classic cognitive profile for adolescents with AN drawing from the current evidence base, as opposed to that observed in adults with AN. This then begs the question of whether there is even a need to assess young people with AN in clinical settings at all, given the time and resources required. While it may be unlikely that a young person with AN will display gross cognitive impairments upon direct testing relating to their AN, what the case series did highlight is the potential range of functioning within this group. Thus, it is vital that eating disorder services providing treatment for adolescents with AN are aware that some of their service users may be experiencing cognitive difficulties; though the root cause of these may be impossible to determine and may not necessarily just be due to AN.

Clinical judgment must be used to determine the need for a neuropsychological assessment at the point of the initial intake AN assessment. This could be achieved through general questioning about cognition with regard to daily functioning, and any changes or longstanding concerns that have been noticed by the young person, and their parents/carers. It may also be also worth questioning about executive functioning abilities in particular, given that these skills are suggested by the adult AN literature as being part of the specific cognitive profile of AN, despite there being no consensus as yet about their picture in younger populations, and so this may be more relevant when assessing older adolescents. Self-report questionnaires about cognitive functioning, such as the BRIEF, may also be useful in helping to determine the clinical significance of any concerns if reported, and deciding whether direct assessment is warranted. As discussed in the review, it would also be important to screen for the presence of any significant mood concerns, using appropriate well-validated and standardized self-report/parental report questionnaires. Depression has been shown to influence

neuropsychological functioning in those few studies that analysed the relationship of mood disorders with neuropsychological functioning in adolescents with AN. Although less is known about the relationship with other co-morbid disorders, such as anxiety, it would be important to consider their impact too on performance.

Conducting a neuropsychological assessment may help inform the formulation and subsequently better tailor the intervention to the needs of that young person if there are cognitive concerns raised, beyond those of poorer concentration that has only emerged since the young person has begun severely under-eating. Given how commonly poorer concentration is reported in AN, and the lack of any gross attentional deficits observed in the studies under review when AN groups were underweight, it is likely that any concentration difficulties result from the impact of starvation and will resolve with improved nutritional intake. An age-appropriate pre-morbid test of intelligence may be worth administering, along with a current measure of intellectual functioning to determine any significant change in overall functioning and also to determine the presence of relative deficits in specific neuropsychological domains. The rest of the testing battery should be guided by the concerns raised at assessment, in order to prevent putting a young person through unnecessary testing when they may fatigue more easily and lack concentration due to their AN. It would also be important to note down and consider the impact of the young person's physical state at the time of testing when interpreting the results, including their BMI/weight-for height, presence of amenorrhea, current daily calorie intake and any prescribed psychoactive medications.

As Meyer and colleagues (2001) propose, one of the main purposes of any psychological assessment is to identify "therapeutic needs, highlight issues likely to emerge in treatment, recommend forms of intervention, and offer guidance about likely outcomes". The results of the neuropsychological assessment should be fed back to the young person and their family, and be built in to the overall formulation of their

presentation. For example, there are some domains of functioning that may be more influenced by physical state and if deficits are present during the acute phase of AN, these may resolve with weight-gain, can can be monitored throughout treatment. As the review did suggest, some domains appeared to be less influenced by the state of AN, suggesting deficits may be pre-morbid and less likely to improve upon full-recovery. This would then necessitate careful thought about how to support the young person if these deficits will persist throughout their lives and cause functional impairment. For example, if set-shifting difficulties and weak central coherence emerge as being clinically significant after testing, Cognitive Remediation Therapy may be worth offering to the young person as part of their treatment package. Psychoeducation should be offered to young people, their carers and educators about how the current neuropsychological profile may impact on the person's functioning, and how best to support them with their individual needs.

Practice-based Evidence

This review drew my attention to the need to collect practice-based evidence as a routine part of clinical practice when working with rare populations such as AN, in order to increase sample sizes, and therefore the statistical power of studies. Having worked in a number of clinical services, I have observed the attitudinal differences within clinical teams to conducting research as part of the routine assessment and treatment protocols. All members of the team must be invested into the long-term outcome of collecting such data and the potential clinical utility of the exercise, to ensure adherence to the protocol and accurate data. However, this is difficult in services where team members are already burdened by high caseloads. Asking clinicians to take on another activity or role on top of their full clinical caseload, without offering additional time to carry this out, is often viewed with frustration and may be seen as

unnecessary. While carrying out this review, many clinicians working in this area advocated for the need for this research. However, this was a time consuming exercise that was only facilitated through having dedicated research days alongside my clinical work. If research agendas within clinical services are to be completed in order to advance the field, clinicians must be allocated protected research time as part of their job roles, allowing for adequate time to conduct all elements of the research process.

Carrying out this research was greatly enhanced by my clinical experience of working in a specialist child and adolescent EDs service. This demonstrated the utility of occupying the scientist-practitioner role, in that I believe that my theoretical knowledge of this field alone would have been insufficient for a thorough interrogation of such studies. My awareness of relevant issues that needed to be considered in the analysis was greatly informed by my clinical experiences. I have learned that I require both clinical and research knowledge for skilled practice in both domains.

Empirical Paper

Recruitment and Attrition

Undertaking this empirical research was a surprising journey from the recruitment stage through to the analysis. During the early stages of planning the research design, my research partner, Jasmin Langdon-Daly and I were asked to anticipate any obstacles that we might have encountered during the research process. One of our main concerns in the early stages was how long it might have taken and how difficult it might have been to recruit a sufficiently sized sample of 5:2 dieters, given that this diet needed to be novel to them. Therefore we used a broad range of advertisement methods when recruiting, including social media methods, to try target as wide a population as possible, as advocated by previous researchers in health research

(Fenner et al., 2012). Not only did we target typical participant groups, such as undergraduate students, but also through specific internet forums, we were able to broadcast our study to a much wider, more relevant population. This was an effective strategy given how quickly we recruited sufficient numbers, and at a more rapid pace than anticipated. On reflection, we were lucky to have been profiled on the front page of the official 5:2 diet forum, "The Fast Diet", for a number of weeks. This forum brought our study to the attention of a large range of people and resulted in the vast majority of participants. Social media is a newer avenue that has the potential to make research participation far more accessible to people than previously. This was illustrated by the interest we received worldwide, including from one individual who was living in Antartica. The level of curiosity in this study from the general public, colleagues and friends was greater than expected. This indicates how widespread the interest is in this diet, and therefore how widely relevant our findings may be. The quick recruitment smoothed the pace of the rest of the study, facilitating ample time for data collection and analyses.

While we quickly recruited people into the study, there was also a very high attrition rate throughout, though this rate was comparable with those reported in studies of other diets. Interestingly, while certain participants failed to complete two cognitive testing sessions in the third and fourth week of the diet, some still managed to complete the final part of Jasmin's study after four weeks, and vice versa. This may suggest that participants were motivated to engage in different aspects of the study; some were interested in the effects of this diet on their mood, while others were interested in how this diet affected their cognitive functioning. One of the downsides of the high drop-out was that it may have been those people who found the diet to have a negative impact on their cognitive functioning dropped out, as some participants did indicate that the 5:2 diet was not compatible with functioning in their daily lives. It would have been

unethical to encourage or incentivise participants to continue dieting if they wished not to; however, failure to do this may have left us with a biased final sample. In the design stage, we did anticipate some attrition and tried to combat this by offering two prize draws, with the higher prizes available upon completion of the study to incentivise participants to complete all aspects of the study. However, as our sample ended up being much older than anticipated and therefore likely to have been more financially stable, perhaps our prize draws were not particularly motivating to our sample. It may have been worthwhile employing a different method of incentivising participant retention, by offering a more suitable reward for this age group.

This experience also underpins the need to recruit much higher numbers initially than a power calculation would anticipate, especially with repeated measures designs, and when using online data collection methods, due to data loss resulting from a less-controlled environment.

Ethical Dilemma

Speaking to participants during screening phone calls, many appeared drawn to the "science" behind the 5:2 diet. Some seemed invested in the other health benefits that were being marketed by its proponents, aside from that of weight-loss. These included the potential benefits of how reducing calorie intake may decrease risks of neurodegenerative diseases (Mosley & Spencer, 2013). My knowledge of the scant literature about the effects of the 5:2 diet specifically and knowledge of the risks of dieting being associated with EDs generally, presented an ethical dilemma during these conversations. On the one hand, participants were already interested in this diet and intent on pursing it outside of our study, but on the other hand, many reported that they believed participating in the study would enable them to stick with the diet in its early stages. I was concerned that I may have been enabling participants to pursue a diet that

may not live up to its claims, as the science about this diet was in its infancy, and additionally, dieting could pose risks to them. Knowing that participants were already committed to starting this diet, and being open about the lack of currently available human studies about these purported benefits, helped resolve this dilemma. I adopted a neutral stance during these conversations, as I was keen not to become an advocate of this diet unwittingly.

Null Findings

"The real purpose of the scientific method is to make sure Nature hasn't misled you into thinking you know something you actually don't know."

Pirsig (1997), p. vii

There was a consistent pattern of non-significant findings throughout on completion of the main analyses, indicating that intermittent fasting using the 5:2 diet did not have any detrimental, or indeed beneficial, impact on the executive functioning of healthy adults in the short-term. My colleague, investigating the effects of the 5:2 diet on mood, eating behaviours, and eating disorder symptomatology (Langdon-Daly, 2016), also did not find any negative effects of this diet over the study period. In fact, her findings suggested this diet appeared to have some positive impacts, especially for those participants with the most risk factors associated with EDs. These findings were a surprise to the research team, even though this study was carried out with the aim of being exploratory as it was the first of its kind. The literature suggests that there is a negative impact on the executive functioning of healthy adults when in acute fasting states, using similar cognitive tasks. This led to an expectation that we would find poorer performance on fasting days, in at least some of the tasks. Given the association between dieting and EDs, we may also have been biased towards predicting a negative outcome from this intermittent fasting diet. Although, it must be said that the evidence

of dieting being a risk factor for eating pathology is somewhat contradictory. One meta-analytic review of this area concluded that dieting may instead attenuate overeating tendencies (Stice, 2002). Our two studies taken together indicate that, despite our hypotheses, perhaps there are no major risks in doing the 5:2 diet from a cognitive or psychological point of view in the short-term.

Doing this research challenged my own long-held biases about the dangers of dieting for everyone. Thinking specifically about the 5:2 diet, it is inherently a flexible diet that does not require continuous calorific deprivation. It also does not advocate cutting out or reducing any major food groups, unlike many other diets. Perhaps there is something unique about the flexibility of the 5:2 diet. Similarly, eating disorder treatment often advocates flexibility around eating within a regular eating pattern as being a goal of treatment. Given that obesity is a big problem in many societies worldwide (James, Leach, Kalamara, & Shayeghi, 2001), there is a need to develop safe weight-loss strategies, which will involve reduction in calorie intake.

Obtaining null findings also raised the issue of the positive publication bias that has been endemic in scientific journals. There have recently been many advocates of the need for peer-reviewed journals to change their stance, and publish non-significant, as well as significant findings. This would bring more balance to the evidence base (Goodchild van Hilten, 2015). Recently a number of new scientific journals explicitly aimed at reporting negative results have been published, such as the *Journal of Negative Results*. It is also argued that researchers themselves must also learn to embrace negative results, not viewing these as "failures" but something that is also worthy of writing up and submitting for publication (Goodchild van Hilten, 2015). This was something that I encountered when I initially completed my analyses, feeling disappointed that my sample performed similarly on fasting and non-fasting days. I was concerned that this would lead to my study being considered less valuable. However,

having considered the meaning of my results within the context of the evidence base, it did demonstrate that these non-significant findings do have some merit in developing our understanding of the impact of nutrition on cognition. By learning that minimal calorie intake does not have the same impact as total restriction on cognition, this brings another important questions to light about the calorie threshold required for the maintenance of cognitive functioning.

Conclusion

This research has taught me the importance of using the scientific method, with regard to challenging biases and expectations. Occupying the researcher role throughout my clinical placements has allowed me to see the benefits of acting in these roles at the same time. They both have positive bidirectional influences on each other. Being a scientist-practitioner leads to more informed research, which in turn leads to better clinical understanding and more informed practice. This enables clinical psychologists to be more effective practitioners in general, and especially when working in more complex areas like EDs.

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APPENDICES

Appendix I

Table A1 - *Bias and Quality Rating of Studies under Review*

ID	Author (Date of Publication)	Selection of Subjects: 1. Exclusion criteria 2. Diagnosis	Comparability of Subjects: 1. Healthy Controls 2. Matched	Ascertainment of Outcome: 1. Standardised tests 2. Control for co-variates 3. Objective report	Bias & Quality Rating	Rank
1	Sarrar et al. (2016)	1. Yes 2. Yes	1. Yes 2. No - unequal groups sizes	1. Yes 2. Yes 3. Yes	**6**	**High**
2	van Noort et al. (2016)	1. Yes 2. Yes	1. Yes 2. Yes - individual case control by age, gender and IQ	1. Yes 2. Yes 3. Yes	**7**	**High**
3	Stedal & Dahlgren (2016)	1. No 2. Yes	1. No 2. No	1. Yes 2. No 3. Yes	**3**	**Medium**
4	Kjaersdam Telléus et al. (2015)	1. No 2. Yes	1. Yes 2. Yes - case control pairs	1. Yes 2. No 3. Yes	**5**	**Medium**
5	Lang et al. (2015)	1. Yes 2. Yes	1. Yes 2. No - frequency matched of age, gender, IQ	1. Yes 2. Yes 3. Yes	**7**	**High**
6	Stedal & Dahlgren (2015)	1. No 2. No	1. No 2. No	1. Yes 2. No 3. Yes	**2**	**Low**
7	Overas et al. (2015)	1. Yes 2. Yes	1. Yes 2. No but same sex, similar age	1. Yes 2. Yes 3. Yes	**6**	**High**
8	Breithaupt, Payne, & Rose (2014)	1. No 2. Yes	1. No 2. No	1. Yes 2. No 3. Yes	**3**	**Medium**
9	Dahlgren et al. (2014)	1. No 2. No	1. No 2. No	1. Yes 2. No 3. Yes	**2**	**Low**

ID	Author (Date of Publication)	Selection of Subjects: 1. Exclusion criteria 2. Diagnosis	Comparability of Subjects: 1. Healthy Controls 2. Matched	Ascertainment of Outcome: 1. Standardised tests 2. Control for co-variates 3. Objective report	Bias & Quality Rating	Rank
10	Fornasari et al. (2014)	1. Yes 2. Yes	1. Yes 2. Yes - Individually matched case-control pairs on age sex race language and IQ	1. Yes 2. Yes 3. Yes	**7**	**High**
11	Lozano-Serra et al. (2014)	1. Yes 2. Yes	1. Yes 2. No - unequal groups sizes, but age equivalent	1. Yes 2. No 3. Yes	**5**	**Medium**
12	Rose et al. (2014)	1. No 2. Yes	1. Yes 2. No - but frequency matched in terms of age, female	1. Yes 2. No 3. Yes	**4**	**Medium**
13	Wierenga et al. (2014)	1. Yes 2. Yes	1. Yes 2. No - unequal groups sizes, but age equivalent	1. Yes 2. No 3. Yes	**5**	**Medium**
14	Zwipp et al. (2013)	1. Yes 2. Yes	1. Yes 2. No - unequal groups sizes, but age equivalent	1. Yes 2. Yes 3. Yes	**6**	**High**
15	Calderoni et al. (2013)	1. Yes 2. Yes	1. Yes 2. Yes: case-control 1:2 pairs	1. Yes 2. Yes 3. Yes	**7**	**High**
16	Dahlgren et al. (2013)	1. No 2. No	1. No 2. No	1. Yes 2. Yes 3. Yes	**3**	**Medium**

ID	Author (Date of Publication)	Selection of Subjects: 1. Exclusion criteria 2. Diagnosis	Comparability of Subjects: 1. Healthy Controls 2. Matched	Ascertainment of Outcome: 1. Standardised tests 2. Control for co-variates 3. Objective report	Bias & Quality Rating	Rank
17	Stedal et al. (2013)	1. Yes 2. Yes	1. Yes 2. No	1. Yes 2. Yes 3. Yes	**6**	**High**
18	Buhren et al. (2012)	1. Yes 2. Yes	1. Yes 2. No- but similar age and gender frequency in group	1. Yes 2. Yes 2. Yes	**6**	**High**
19	Fitzpatrick et al. (2012)	1. Yes 2. Yes	1. Yes 2. No, but similar in age, gender	1. Yes 2. No 3. Yes	**5**	**Medium**
20	Frampton et al. (2012)	1. No 2. Yes	1. Yes 2. Yes: Case control- IQ and gender matched	1. Yes 2. No 3. Yes	**5**	**Medium**
21	Rose et al. (2012)	1. No 2. Yes	1. No 2. No	1. Yes 2. No 3. Yes	**3**	**Medium**
22	Shott et al. (2012)	1. No 2. Yes	1. Yes 2. No, but similar educational level	1. Yes 2. Yes 3. Yes	**5**	**Medium**
23	Stedal et al., (2012)	1. Yes 2. Yes	1. No 2. No	1. Yes 2. Yes 3. Yes	**5**	**Medium**
24	Andres-Perpina et al., (2011)	1. Yes 2. Yes	1. Yes 2. No - but age is similar across groups	1. Yes 2. Yes 3. Yes	**6**	**High**
25	Dmitrzak-Węglarz et al. (2011)	1. Yes 2. Yes	1. Yes 2. No	1. Yes 2. No 3. Yes	**6**	**High**

ID	Author (Date of Publication)	Selection of Subjects: 1. Exclusion criteria 2. Diagnosis	Comparability of Subjects: 1. Healthy Controls 2. Matched	Ascertainment of Outcome: 1. Standardised tests 2. Control for co-variates 3. Objective report	Bias & Quality Rating	Rank
26	McAnarney et al. (2011)	1. Yes 2. Yes	1. Yes 2. No, but matched at group level for age, ethnicity, SES and IQ	1. Yes 2. Yes 3. Yes	**6**	**High**
27	Nagamitsu et al. (2011)	1. Yes 2. Yes	1. Yes 2. No but age similar group level	1. No 2. No 3. Yes	**4**	**Medium**
28	Sarrar et al. (2011)	1. No 2. Yes	1. Yes 2. Yes	1. Yes 2. Yes 3. Yes	**6**	**High**
29	Hatch et al., (2010)	1. Yes 2. Yes	1. Yes 2. No, but sex, age and education matched at group level	1. Yes 2. Yes 3. Yes	**6**	**High**
30	Castro Fornieles et al. (2009)	1. No 2. Yes	1. Yes 2. Yes	1. Yes 2. No 3. Yes	**5**	**Medium**
31	Neumarker et al. (2000)	1. No 2. Yes	1. Yes 2. Yes	1. Yes 2. No 3. Yes	**5**	**Medium**
32	Blanz et al. (1997)	1. Yes 2. Yes	1. No 2. Yes - PC case-control pairs	1. Yes 2. No 3. Yes	**5**	**Medium**
33	Bradley et al. (1997)	1. Yes 2. Yes	1. Yes (unclear as no ED, but recruited from medical centre and "normal" but unclear if healthy 2. Yes - case	1. Yes 2. No 3. Yes	**6**	**High**

ID	Author (Date of Publication)	Selection of Subjects: 1. Exclusion criteria 2. Diagnosis	Comparability of Subjects: 1. Healthy Controls 2. Matched	Ascertainment of Outcome: 1. Standardised tests 2. Control for co-variates 3. Objective report	Bias & Quality Rating	Rank
			control pairs for age, SES, and vocab			
34	Dura & Bornstein (1989)	1. No 2. Yes	1. No 2. No	1. Yes 2. No 3. Yes	**2**	**Low**
35	Witt et al., (1985)	1. No 2. Yes	1. Yes 2. Yes - case control by age, education and IQ	1. Yes 2. Yes 3. Yes	**6**	**Medium**
36	Wilbur & Collegian (1981)	1. No 2. Yes	1. No 2. Yes - case-control matched psychiatric control group	1. Yes 2. No 3. Yes	**4**	**Medium**
	High	6-7				
	Medium	3-5				
	Low	1-2				

Appendix II

Table AII - *Domains of Functioning and Corresponding Tasks Used*

Domain of Functioning	**Sub-domain**	**Test Battery**	**Tasks Used**
Intelligence		Culture Fair Intelligence Test 1/2 (1, 28, 31), Wechsler Abbreviated Scales of Intelligence (WASI) (3, 5, 6, 8, 12, 13, 20, 23, 21), Wechsler Adult Intelligence Scales R/III (WAIS R/III)/Wechsler Intelligence Scale for Children R/III (WISC R/I) (4, 6, 7, 9, 11, 15, 18, 19, 23 , 36), Raven Standard Progressive Matrices (10), Kaufman Brief Intelligence Test-2 (26), Spot the word test (29), Prufsystem fur Schul-und-Bildungsberatung (PBS (32) and Peabody IQ	

Processing Speed	Wechsler Scales, CANTAB (4), and IntegNeuro battery (29)	Digit Symbol (1, 33, 35), Coding F task (33), Trail Making Test a (1, 4, 11, 14, 28), Rey Complex Figure Test (time to copy) (RCFT; 11, 24, 30), Simple and Choice Reaction Time subtest (4), Choice reaction time (29) and Tapping subtests (29)
Attention	CANTAB (4), IntegNeuro test battery (29), NEPSY-II (15), Wechsler Scales (30), PBS (32)	Rapid Visual Information Processing, TMT a (11,14), Switching of Attention, Sustained Attention, Go-no-Go and Auditory Oddball (29), Auditory Attention (15), Digit Span and Coding (30), attentional subtests 9&10 (32), Dichotic Words and Continuous Performance Test (33)
Executive Functioning	NEPSY-II, D-KEFS	

	Inhibitory Control	IntegNeuro battery (29), NEPSY II (15), and D-KEFS (3, 8, 16, 19, 20, 21, 23)	Stroop task (11, 24), Verbal interference and Go-no-Go subtests (29), Response Set and Inhibition (15), Colour-Word Interference (3, 8, 16, 19, 20, 21, 23), Hayling Test (8, 20, 21)
	Cognitive Flexibility	D-KEFS (2, 3, 4, 6, 8, 11, 16, 19, 20, 21, 23, 24, 35), NEPSY-II (15), ANTP (18), CANTAB (4, 26)	Wisconsin Card Sorting Test (1, 5, 7, 11, 13, 19, 24, 25, 26), Trail Making Test (part b or condition 4 from D-KEFS; 2, 3, 4, 6, 8, 11, 16, 19, 20, 21, 23, 24, 35), Animal Sorting (15), the Visual Set-shifting Task (18), the Novel category learning task (22), the Brixton Test (6, 16, 19, 23), Intra-Extra Dimensional Set Shift (4, 26), probabilistic Object Reveral Task
	Decision Making		Iowa Gambling Task (10)
	Planning	CANTAB (4), IntegNeuro (29), NEPSY II (15)	Tower Task (3, 6, 16, 20, 21, 23), Stockings of Cambridge (4), Maze and Timing subtests(29) and

			Clocks (15)
	Central Coherence	Wechsler Scales (11)	Central Coherence Index score from Rey-Osterrieth Complex Figure Test (2, 3, 5, 6, 12, 16, 21, 23), Block Design (11), the Group Embedded figures task (16), Fragmented Pictures task
	Working Memory	Wechsler scales (30, 35), IntegNeuro (29), NEPSY-II (15) and CANTAB (4)	Digit Span (29/30, 35), Word List Interference(15), Symbol-Digit Learning Test (SDLT) (35), Span of Visual Memory(29), Spatial Span and Spatial Working Memory (4), and n-back task (10)
	Verbal Fluency	D-KEFS (3, 6. 8. 16, 17, 19, 20, 21, 23), NEPSY-II (15), IntegNeuro battery (29)	Verbal Fluency (3, 6. 8. 16, 17, 19, 20, 21, 23), Word Generation (15), IntegNeuro battery (29), Controlled Oral Word Association Test (24), Word Fluency (Japanese version) (27)

Visuospatial Abiltiy	Visual Object and Space Perception battery (20), Wechsler scales (30), NEPSY-II (15)	accuracy of copy in the RCFT (4, 12, 24), Silhouettes from the Visual Object and Space Perception battery (20), Block Design from the Wechsler scales (30), Arrows, Block Construction, Design Copying, Geometric Puzzles, Picture Puzzles and Route Finding from the NEPSY-II (15), and Visual Search Test (33), Mental Rotation Task (33), Judgement of Line Orientation (33), Card Rotations Test (33), and Perceptual Closure Test (33)
Verbal Ability	Wechsler scales (various editions of the WAIS, WISC and WASI:4, 6, 7, 8, 9, 11, 17, 21, 23, 30, 36, 4, 13, 30, 36), CFT battery (31) PBS (32), NEPSY-II (15)	Vocabulary (4, 6, 7, 8, 9, 11, 17, 21, 23, 30, 36) and Similarities (4, 13, 30, 36), Vocabulary (31), Verbal subtests 1, 2, 5 &6, Comprehension of Instructions, Oromotor Sequences, Phonological Processing, Repetition of Nonsense Words,

			Speeded Naming, Word Generation (15)
Memory	Verbal Memory	Tests of Memory and Learning 2nd Edition (4), List Memory, NEPSY II (15), IntegNeuro test battery (29), Wechsler Memory Scales (24), Denman Neuropsychological Memory Scales (33).	Memory for Stories - Immediate and Delayed subtests (4), List Memory, Memory for Names, Narrative Memory and Sentence Repetition (15), Verbal Learning and Recall (29), Logical Memory I&II (24), Rey Auditory Verbal Learning Test (RAVLT) - immediate recall (24) and Verbal scales (33).

	Visual Memory	Wechsler Memory Scales (11, 24, 35), NEPSY II (15), Denman Neuropsychological Memory Test (33)	immediate and delayed recall measure of RCFT (3, 6, 11, 12, 16, 20, 21, 23, 24, 30), Pattern Recognition Memory and Spatial Recognition Memory (4), Visual Reproductions - immediate and delayed conditions (11, 24, 35), Memory for Designs and Memory for Faces - immediate and delayed recall conditions (15), the Nonverbal Scale (33)
Academic Ability		Wide Range Achievement Tests (13, 34)	Reading (13, 34), Arithmetic (34)), Spelling (34)

- Please note that the numbers in the table refer to the Study ID number

Appendix III

Details of Collaboration in a Joint Thesis

The empirical research outlined in this thesis was undertaken as part of joint project with Jasmin Langdon-Daly, another trainee clinical psychologist in the same cohort at UCL. Her research involved investigating participants' mood, eating behaviours and eating disorder symptomology before beginning the 5:2 diet and after 4 weeks of dieting, using a repeated measures design. Please refer to her thesis submission for further details.

Aspects of research undertaken independently:

- Review of relevant literature
- Research proposal
- Selection of outcome measures
- Study design for individual project
- Data collection, extraction and processing
- Data analysis
- Write up of empirical paper

Aspects of research undertaken jointly:

- Planning procedure of overall study
- Research governance tasks (application for ethical approval, funding, risk assessment, data protection)
- Recruitment and screening of participants
- Correspondence with participants

Appendix IV

Letter Granting Ethical Approval

UCL RESEARCH ETHICS COMMITTEE
ACADEMIC SERVICES

Dr Lucy Serpell
Department of Clinical, Educational and Health Psychology
UCL

28 January 2015

Dear Dr Serpell

Notification of Ethical Approval
Project ID 6377/001: Investigating the impact of intermittent fasting diets on cognition, behaviour and emotional well-being

I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that your study has been approved by the UCL REC for the duration of the project i.e. **until September 2016.**

Approval is subject to the following conditions:

1. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form': http://ethics.grad.ucl.ac.uk/responsibilities.php

2. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. Both non-serious and serious adverse events must be reported.

   Reporting Non-Serious Adverse Events
   For non-serious adverse events you will need to inform Helen Dougal, Ethics Committee Administrator [redacted] within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair of the Ethics Committee will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

   Reporting Serious Adverse Events
   The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

On completion of the research you must submit a brief report (a maximum of two sides of A4) of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

Appendix V

Advertisement used for Recruitment

UCL

Are you thinking of starting the 5:2 Diet?

Are you curious about the impact it has on thinking, feelings or behaviour?
Would you like to help us find out more?

We are researchers in the department of Clinical, Education and Health Psychology at UCL, looking to understand more about the psychological effects of the 5:2 diet/ intermittent fasting in healthy adults. We will be investigating the diet's impact on mood, cognition (thinking), and eating behaviour. We would like to compare how people answer certain questions before and after starting the diet, and how they perform on certain online tasks on fasting and non-fasting days.

We are looking for people (aged 18-65) who have not yet started the 5:2 diet, but intend to do so for at least a month, to take part in our research. Participation will involve completing questionnaires, and doing online experimental tasks. You can participate from anywhere as the study can be completed online and over the phone.

All participants will be entered into a prize draws to win Amazon vouchers. There will be 12 vouchers in total to be won (ranging from £20-£100). For each person taking part in the study we will also donate £1 to charity and, and you will be able to vote for the charity this money goes to. Once we have completed the study, all participants will also receive a summary of the findings.

If you think you might be interested in taking part, or would like more information, please contact us to find out more:

[redacted]

We look forward to hearing from you,

Jasmin Langdon-Daly and Kate Mahony
UCL DClinPsy Programme
Twitter: https://twitter.com/psychgeeks

Appendix VI

Information Sheet for Interested Individuals

Information Sheet for Interested Participants
Investigating the Impact of Intermittent Fasting (5:2) Diets on Cognition, Behaviour and Emotional Wellbeing

This study is approved by the UCL Research Ethics Committee (Project ID Number): 6377/001

Name and Contact Details:	Jasmin Langdon-Daly & Kate Mahony [redacted] Dr Lucy Serpell
Work Address:	Research Department of Clinical Educational and Health Psychology 1-19 Torrington Place, University College London, London WC1E 7HB

We would like to invite you to participate in this research project. You may be able to participate if you are an adult who is about to start the 5:2 diet. You should only participate if you want to. Before you decide whether you want to take part, it is important for you to read the following information carefully. If anything is not clear or if you would like more information, please contact us on the email addresses above.

Information for participants

The 5:2 diet is a form of intermittent fasting: one eats normally for five days per week and reduces calorie intake to 25% of normal requirements, usually 500 calories per day, for two days per week. Although the 5:2 diet is gaining popularity, there is not much research on its impact on people's thoughts, feelings and abilities. The aim of this study is to find out about the impact of starting the 5:2 diet on mood, eating behaviour and ability to do certain mental tasks.

We are looking for healthy adults (18-65 yrs) who are planning to start the 5:2 diet but have not yet begun, to take part in our study.

We would like to compare how people answer certain questions before and after starting the diet, and how they perform on certain online tasks on fasting and non-fasting days. If you decide to participate, before you start the diet we will ask you to complete a food diary for one week and fill out a series of questionnaires online which will ask about your mood, eating behaviours, self-esteem and thinking about food, shape and weight (around 15 minutes). Once you have begun dieting, we will then ask you to complete online tasks (lasting about 20 minutes) at least twice, on different days. After one month of dieting, you will be asked to complete the same food diary and similar questionnaires again.

As an acknowledgement of your contribution participants will be entered into a prize draw to win Amazon vouchers once you have completed the baseline measures. Upon finishing the study, you will be entered into another draw to win more prizes. There will be 12 vouchers in total to be won (£20-£100). For each person taking part in the study we will also donate £1 to charity and, and you will be able to vote for the charity this money goes to. Once we have completed the study, all participants will also receive a summary of the findings.

It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw from the study at any time during the testing session and without giving a reason. This will not affect your rights in any way.
If you would like to take part, please read the consent form below, and if you agree to the terms then please sign to indicate your consent. After this, you will be asked to choose a date to start the diet and be sent instructions about the next steps. You will be contacted by the researchers to remind you to complete the various steps, and can contact us at any point with questions.

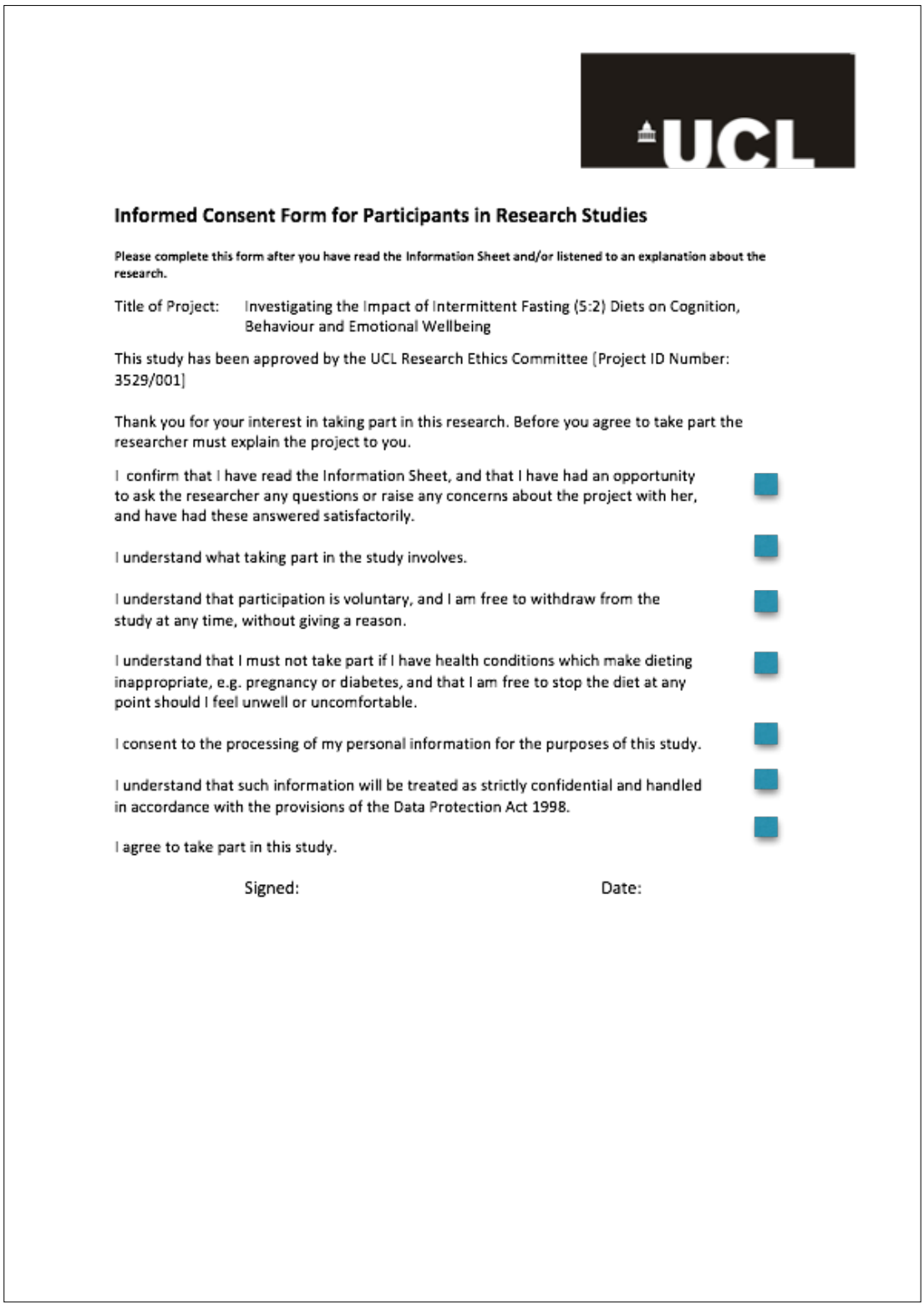
All information provided (along with your personal details) will be kept confidential, and anonymised. Your personally identifiable details will not be linked to your individual responses. No information about you will be disclosed to a third party.

Your participation will contribute significantly to our understanding regarding dieting and psychological well-being. Thank you very much for your time.

All data will be collected and stored in accordance with the Data Protection Act 1998.

Appendix VII

Informed Consent Form



UCL

Informed Consent Form for Participants in Research Studies

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Project: Investigating the Impact of Intermittent Fasting (5:2) Diets on Cognition, Behaviour and Emotional Wellbeing

This study has been approved by the UCL Research Ethics Committee [Project ID Number: 3529/001]

Thank you for your interest in taking part in this research. Before you agree to take part the researcher must explain the project to you.

I confirm that I have read the Information Sheet, and that I have had an opportunity to ask the researcher any questions or raise any concerns about the project with her, and have had these answered satisfactorily. ☐

I understand what taking part in the study involves. ☐

I understand that participation is voluntary, and I am free to withdraw from the study at any time, without giving a reason. ☐

I understand that I must not take part if I have health conditions which make dieting inappropriate, e.g. pregnancy or diabetes, and that I am free to stop the diet at any point should I feel unwell or uncomfortable. ☐

I consent to the processing of my personal information for the purposes of this study. ☐

I understand that such information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998. ☐

I agree to take part in this study. ☐

Signed: Date:

Appendix VIII

Study Instructions for Participants

Appendix IX

Email Correspondence with Participants

1. Initial email to interested individuals

Dear XXXX,

Thank you for contacting us to let us know that you are interested in taking part in our intermittent fasting study using the 5:2 Fast diet at University College London (UCL Project ID 6377/001).

We are currently looking for people who have not yet started the diet to participate, as we are asking participants to fill out a food diary for 7 days before beginning the diet. Our recruitment is ongoing, so once we have spoken over the phone, participants can start as soon as they want (allowing for a week of a food diary).

Please find attached an information sheet, along with a diagram that shows how the study would run. As all of the study tasks take place online, people living outside of the UK can participate.

Please note our inclusion and exclusion criteria for participation below:

- Aged between 18 and 65 years old
- Sufficient level of English language and computer literacy to complete the study
- Normal or corrected to normal visual acuity
- No current or past history of eating disorders (In line with NHS advice).
- No current diagnosed mental health problem.
- Not currently pregnant, or with health conditions such as diabetes where medical advice indicates that fasting would potentially endanger your health
- No specific learning difficulties (such as dyslexia or dyscalculia) or global intellectual disability

It would be great if we could arrange a time to give you more information on the phone and help you decide whether you would like to take part. Please send us a range of suitable times to call you, along with your phone number (or Skype details if you live outside of the UK). We will get back to you as soon as possible to confirm a time.

If you have any questions, please contact us on this email or we can discuss these when we speak on the phone.

Please note that you do not have to decide straight away whether you want to take part.

Best wishes,

Jasmin and Kate

Trainee Clinical Psychologists
UCL DClinPsy Programme
1-19 Torrington Place
London WC1E 7HB
Email: [redacted]
Twitter: **https://twitter.com/psycheeks**

2. Email detailing study instructions

Dear XXXX,

Thank you very much for agreeing to give your time to take part in our intermittent fasting study. Remember that you can decide that you no longer wish to take part at any point in the future without having to give a reason.

Attached to this email is a document which has an outline of the whole study so you have a clear idea of what you will need to do and when. We will also email you to remind you when you need to complete the next part of the study. All of the study can be completed online, via the links that we send you.

The first thing that you need to do is complete the Consent Form, and email back to us as soon as you can (either a scanned copy of this completed form or fill it in using an electronic signature).

We agreed that you would begin the food diary today, **Thursday on 21st May 2015**, complete the first set of questionnaires on W**ednesday, 28th May 2015** and then start following the intermittent fasting 5:2 diet the day after that on **Thursday 29th May 2015**. You are free to follow the diet in the way that you choose, and to decide which two days of the week you wish to 'fast' (meaning limiting your intake to 500cals for women and 650 cals for men). We would ask you to complete the first set of cognitive tasks on a Non-Fasting day, and the second set on a Fasting day in the evening (6-10pm) at the same time each time.

You have been assigned the participant number XXX. Please use this number whenever you complete part of the study, and do not use your name. This will help us to link your data together while ensuring that it remains anonymous and secure. When password protecting documents, the password is: diet .

We have attached a blank food diary. Could you please fill this in in the week up until you complete the first set of questionnaires, when there will be an opportunity to submit it. Please write your participant number but not your name on this diary.

In the meantime, please use this Doodle Poll to vote for the charity that you would like us to make the donation to at the end of the study. We will donate £1 for each participant to the charity receiving the most votes:

https://doodle.com/6vmee26rtct6u3pe

If you have any questions or concerns, or feel that you need more information to help you complete the study, please do not hesitate to get in contact with us.

Thank you again for your help,
Jasmin and Kate

Trainee Clinical Psychologists
UCL DClinPsy Programme
1-19 Torrington Place
London WC1E 7HB

3. Email instructing participants to begin doing cognitive tasks

Hello XXXX,

Thank you for continuing to participate in our study.You should have been following the 5:2 intermittent fasting diet for at least two weeks by now.

It is now time for you to complete the cognitive tasks online as part of our study, by clicking on the weblink below (or copying and pasting the link into your browser), and following the instructions. These should take you between 20-25 minutes to complete online. Please make sure that you enter your participant number, which is 051.

Remember we want you to do these tasks at least twice, on two days over the next two weeks. You must do the first set of tasks on a FASTING day, and the second set of tasks on a NON-FASTING day.

If you would like to do them again after this, please do the third set on a FASTING day, and the fourth set on a NON-FASTING day. Please note that these task orders are different for each participant.

Please follow these instructions when completing the tasks:

- Do these tasks in the evening time between 6-10pm (your own timezone) and at approximately the same time of day each testing session (give or take about 30 minutes).
- Do these tasks in a quiet area, free of potential distractions/interruptions, and complete them in one sitting.
- Please eat something 30 minutes before starting the tasks each time. On fasting days, please consume at least half of your restricted calorie intake before starting the tasks.
- Do not eat any food or consume any calorific drinks during task completion (drinking water is fine).
- Use the same computer and internet browser each time you do the tasks. Please ensure your internet connection is working.
- Do not refresh the webpage once you have begun the tasks as this will bring you back to the opening page.

Please read the online instructions carefully for each of the tasks, as you will not be able to return to them once you have started the task. There will be an opportunity to practise most tasks before doing the real thing.

http://www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=XXX

If there are any further questions, please email us and we will get back to you as soon as possible.

Many thanks,
Jasmin and Kate

Trainee Clinical Psychologists
UCL DClinPsy Programme
1-19 Torrington Place
London WC1E 7HB
Email: [redacted]
Twitter: **https://twitter.com/psycheeks**

4. Reminder email instructing participants to complete cognitive tasks

Hello XXXX,

Thank you for continuing to participate in our study.You should have been following the 5:2 intermittent fasting diet for at least three weeks by now.

It is now time for you to complete the second food diary for the next 7 days using the same template below as previously (see attachment), while continuing to follow the diet.

If you have not yet done so, please ensure that you have completed the cognitive tasks online at least twice using the instructions below over the next 7 days. Please click on the weblink (or copying and pasting the link into your browser). Please make sure that you enter your participant number, which is 120. Please note you can only complete these tasks on a computer or laptop (Mac or PC), but you cannot do them on a tablet, iPad or smart phone device.

http://www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=XXX

Remember you must do the first set of tasks on a NON-FASTING day, and the second set of tasks on a FASTING day. If you would like to do them two more times, please follow the same order.

Please follow these instructions when completing the tasks:

- Do these tasks in the evening time between 6-10pm (your own timezone) and remember to do them within 30 minutes of that specific time the subsequent times you do them.

- Ensure you do these tasks in a quiet area, free of potential distractions/interruptions, and complete them in one sitting.
- Please eat something 30 minutes before starting the tasks each time. On fasting days, please consume at least half of your restricted calorie intake before starting the tasks.
- Do not eat any food or consume any calorific drinks during task completion (drinking water is fine).
- Use the same computer and internet browser each time you do the tasks. Please ensure your internet connection is working.
- Do not refresh the webpage once you have begun the tasks as this will bring you back to the opening page.

Please read the instructions carefully for each of the tasks, as you will not be able to return to them once you have started the task. There will be an opportunity to practise most tasks before doing the real thing.

If there are any further questions, please email us and we will get back to you as soon as possible.

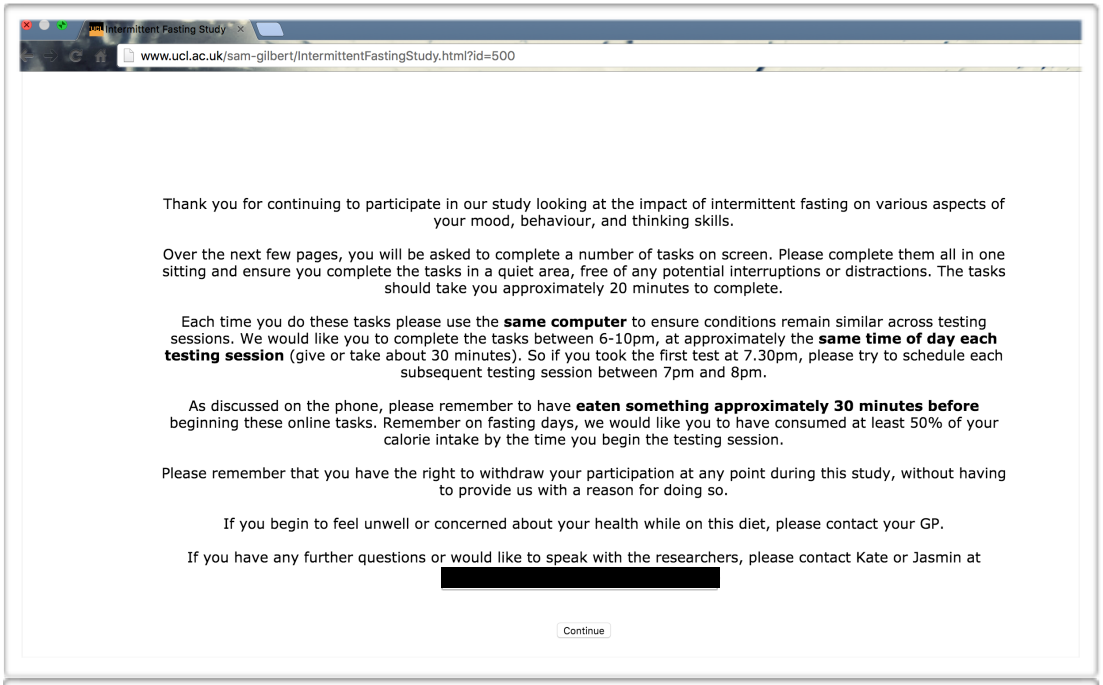
Many thanks,
Jasmin and Kate

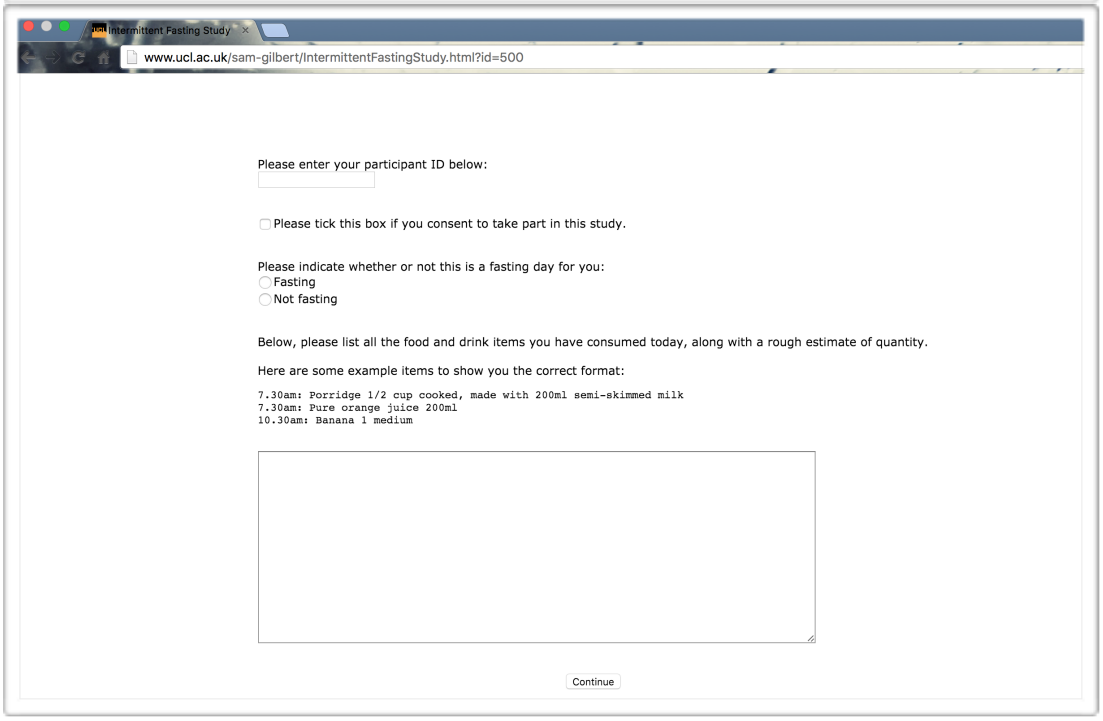
Trainee Clinical Psychologists
UCL DClinPsy Programme
1-19 Torrington Place
London WC1E 7HB
Email: [redacted]
Twitter: https://twitter.com/psycheeks

Appendix X

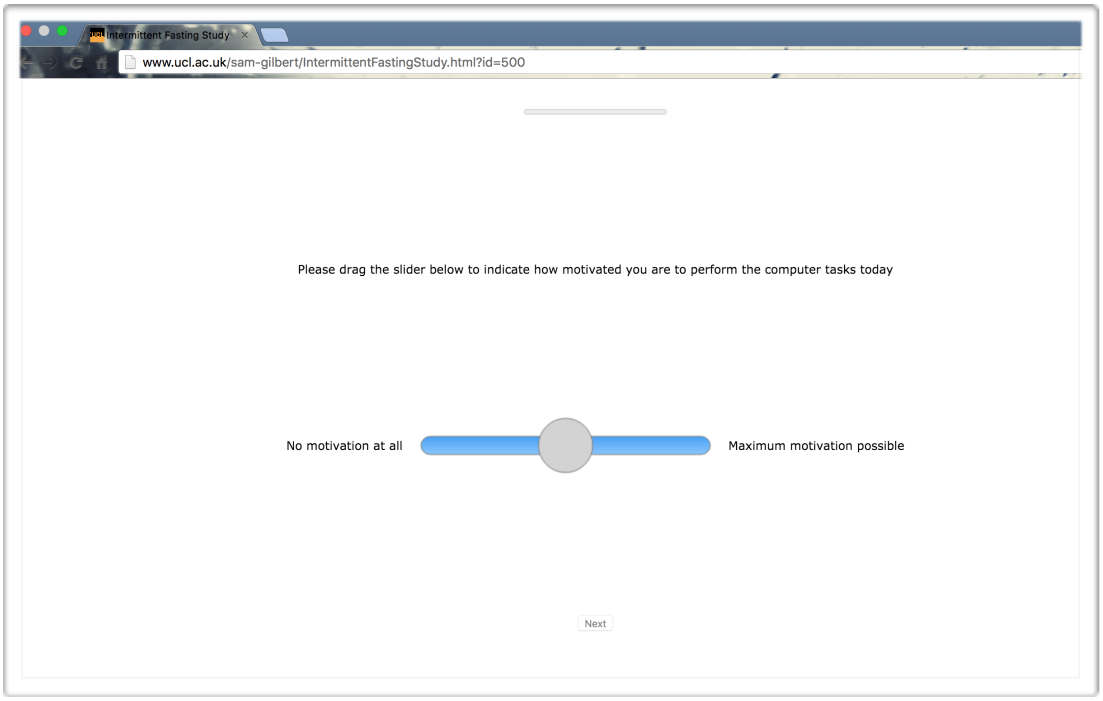
Online Tasks

1. Opening webpages

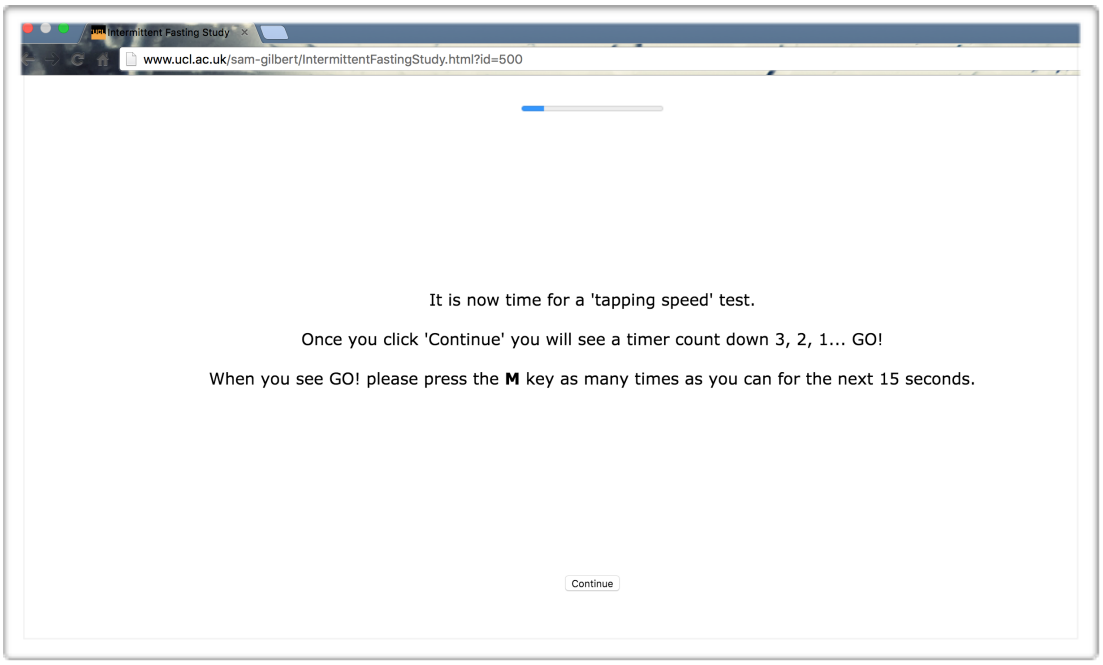




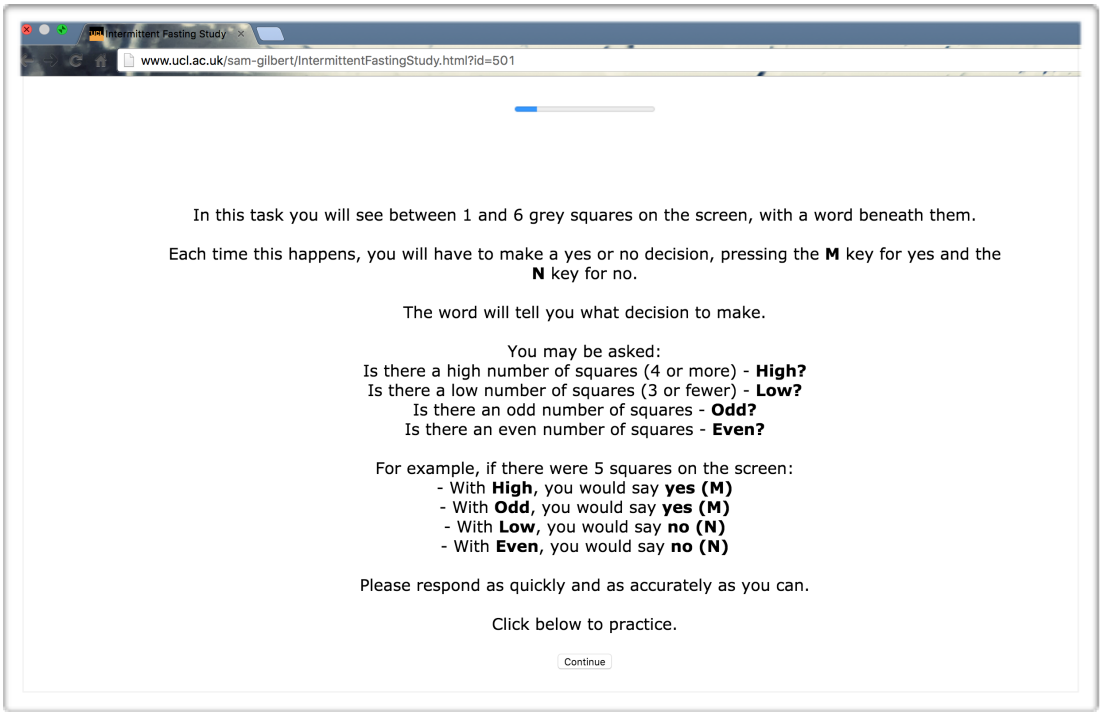
2. Self-reported motivation or effort scale

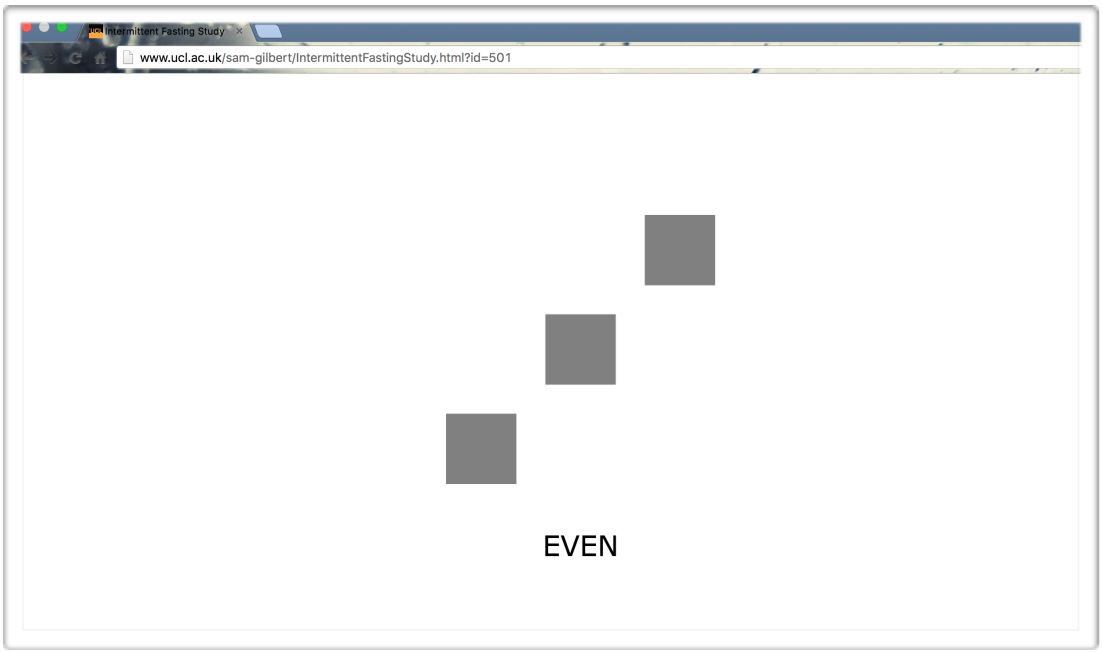


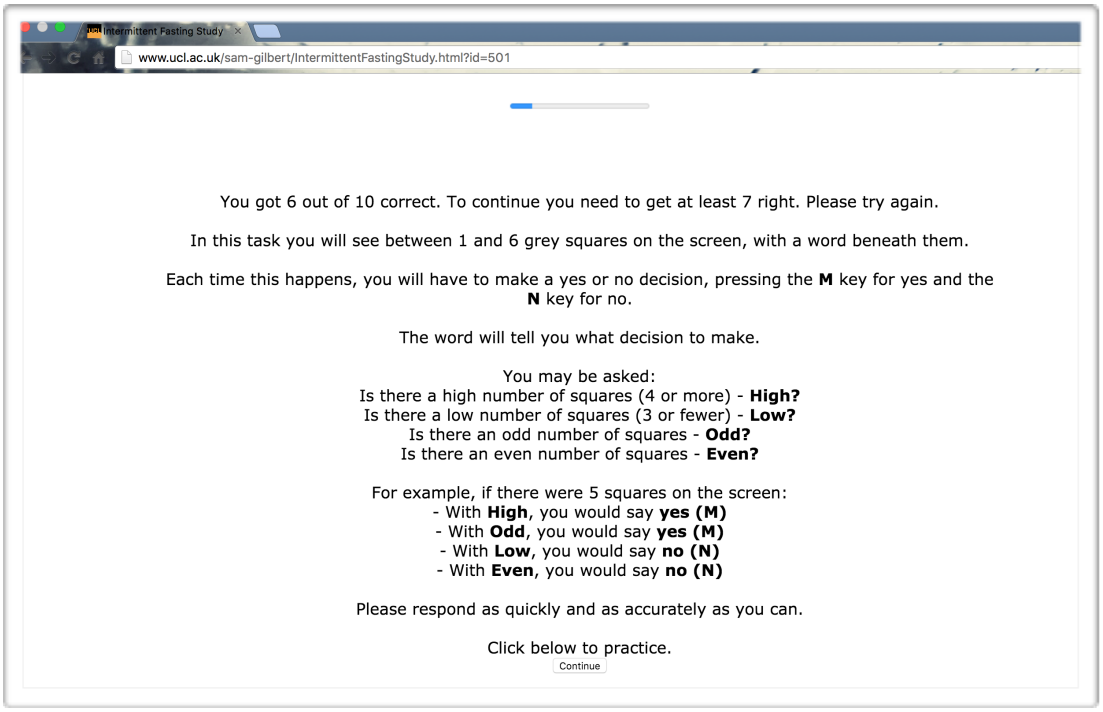
3. Tapping speed x 2

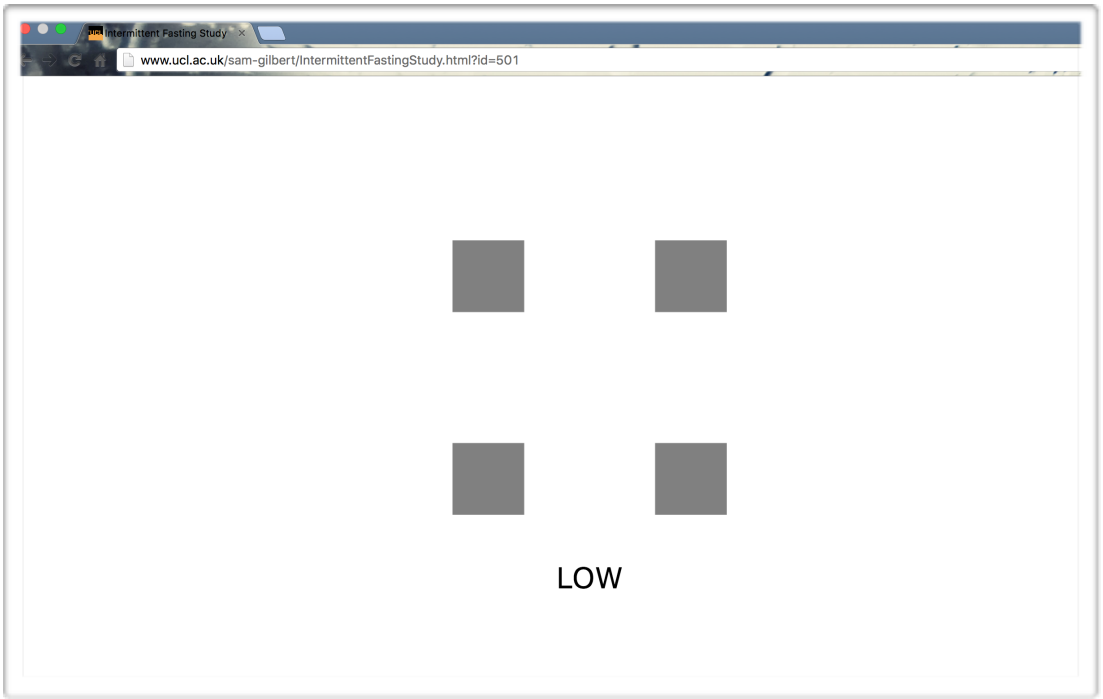


4. Rule Change Task

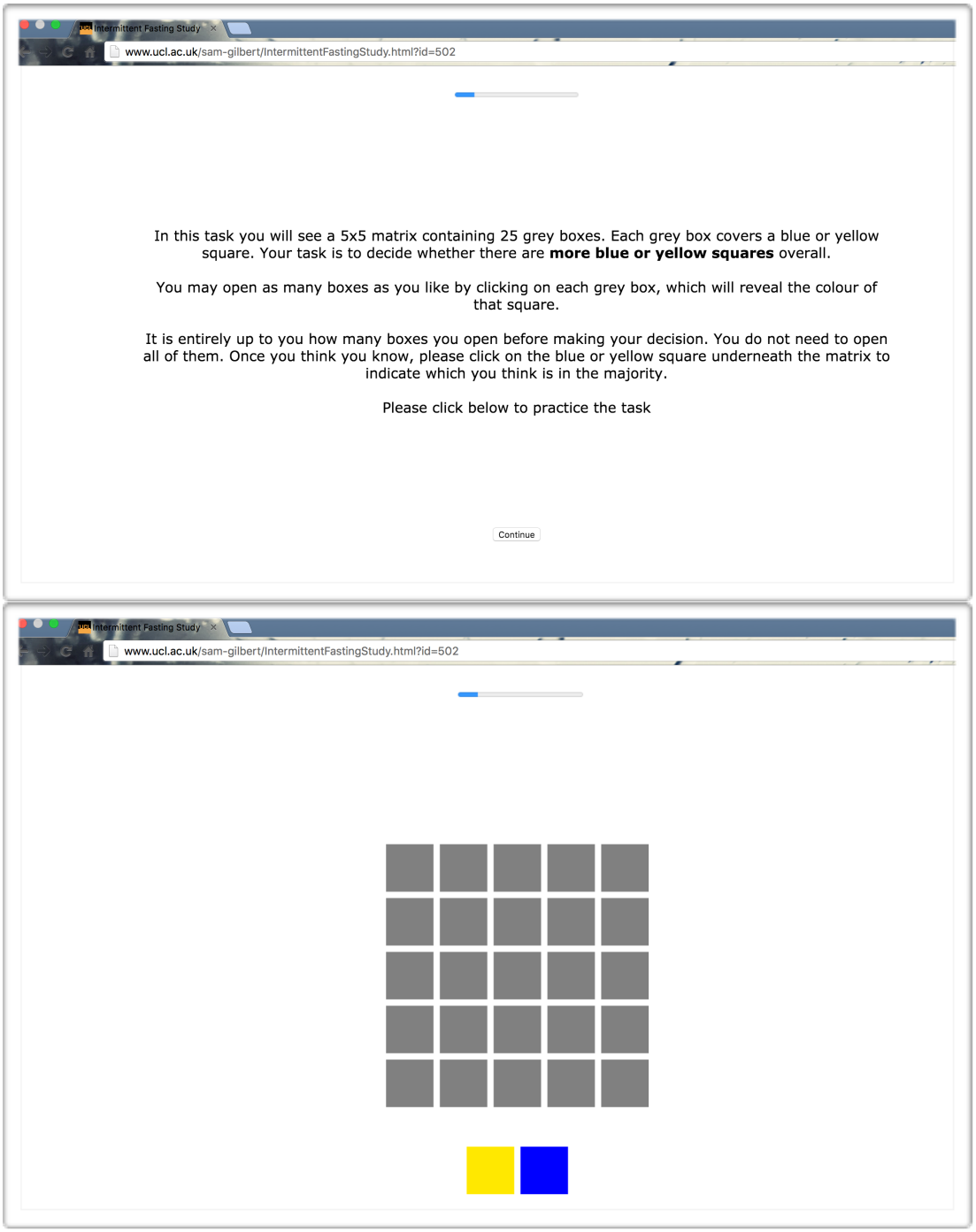


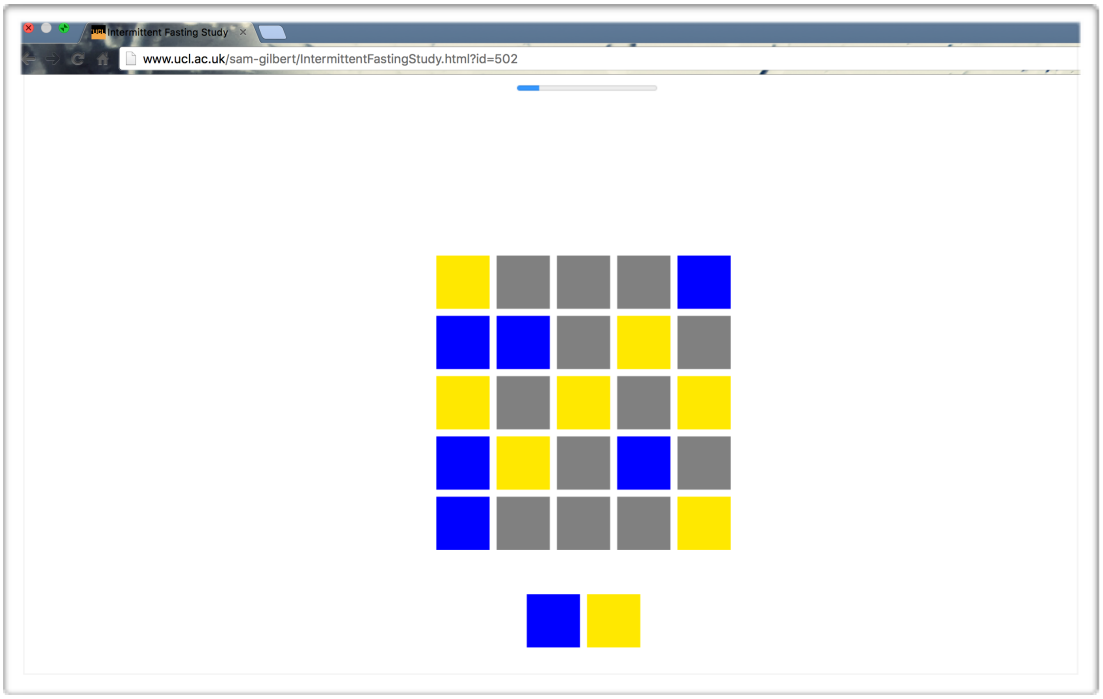



Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=501
You got 6 out of 10 correct. To continue you need to get at least 7 right. Please try again.
In this task you will see between 1 and 6 grey squares on the screen, with a word beneath them.
Each time this happens, you will have to make a yes or no decision, pressing the M key for yes and the N key for no.
The word will tell you what decision to make.
You may be asked:
Is there a high number of squares (4 or more) - High?
Is there a low number of squares (3 or fewer) - Low?
Is there an odd number of squares - Odd?
Is there an even number of squares - Even?
For example, if there were 5 squares on the screen:
- With High, you would say yes (M)
- With Odd, you would say yes (M)
- With Low, you would say no (N)
- With Even, you would say no (N)
Please respond as quickly and as accurately as you can.
Click below to practice.
Continue

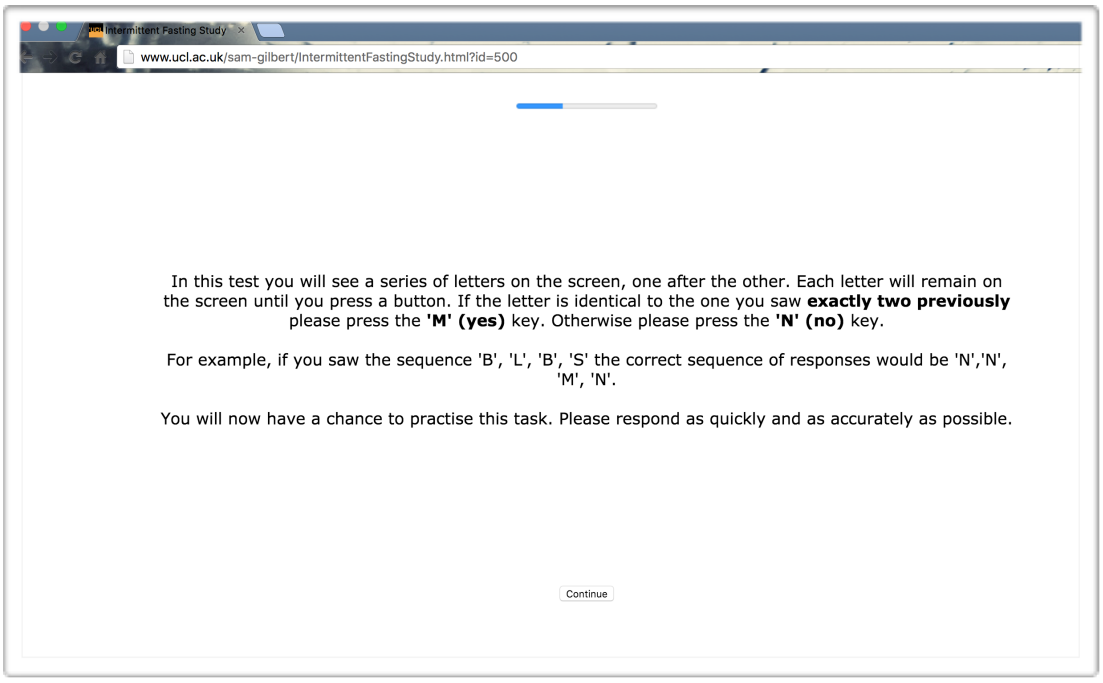

Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=501
LOW

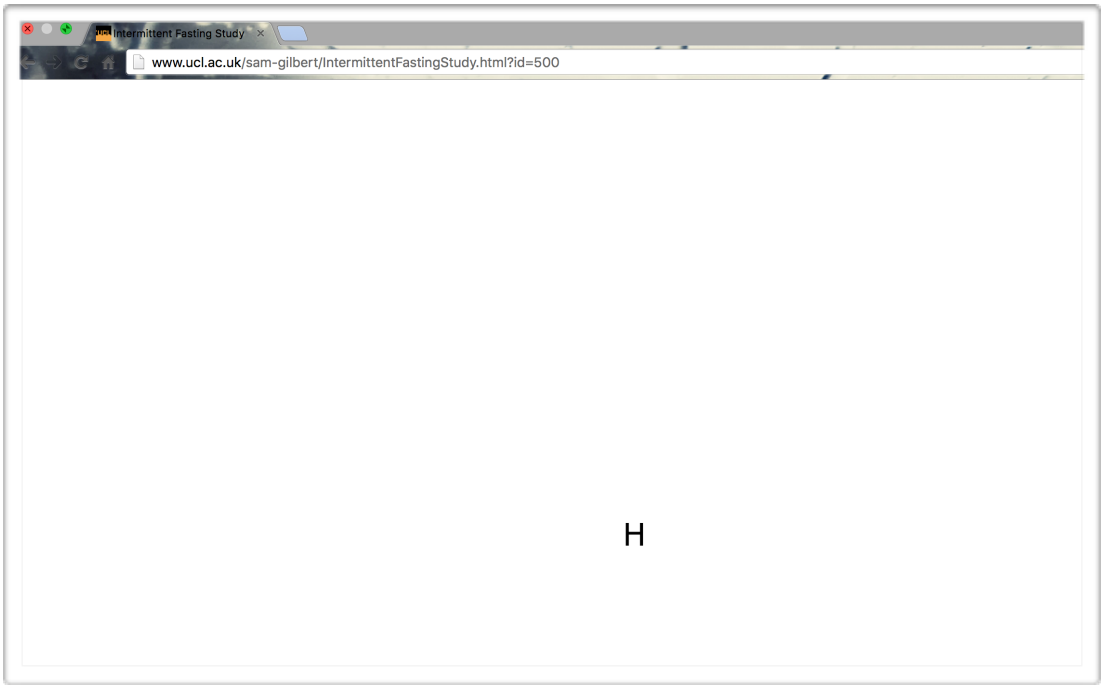
5. Information sampling task

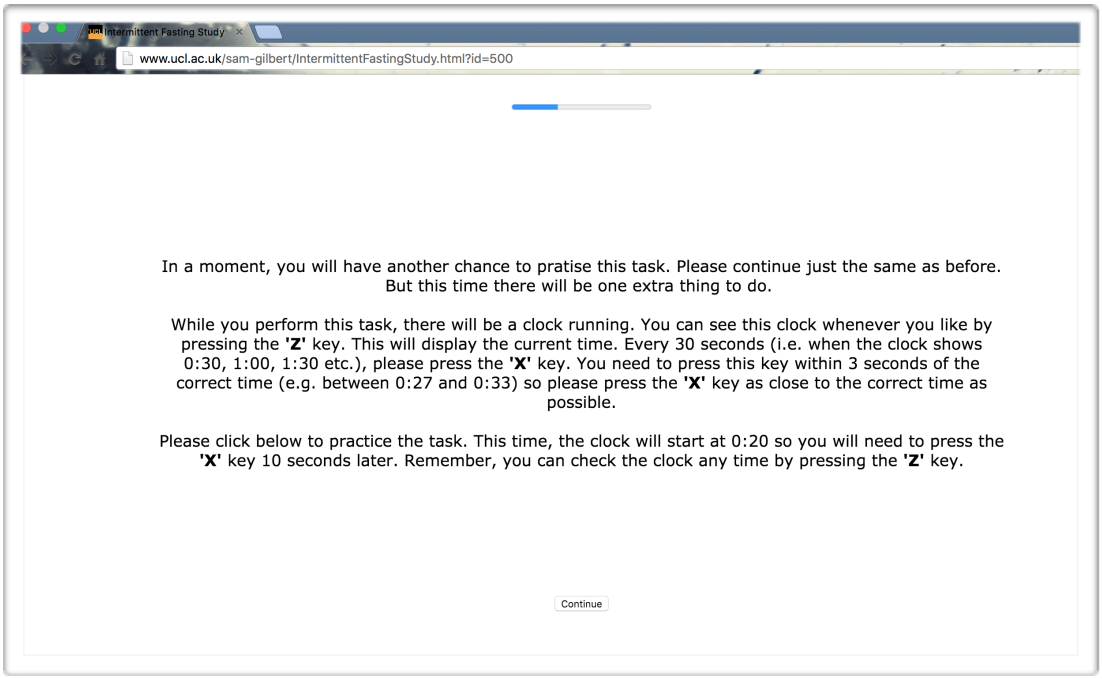


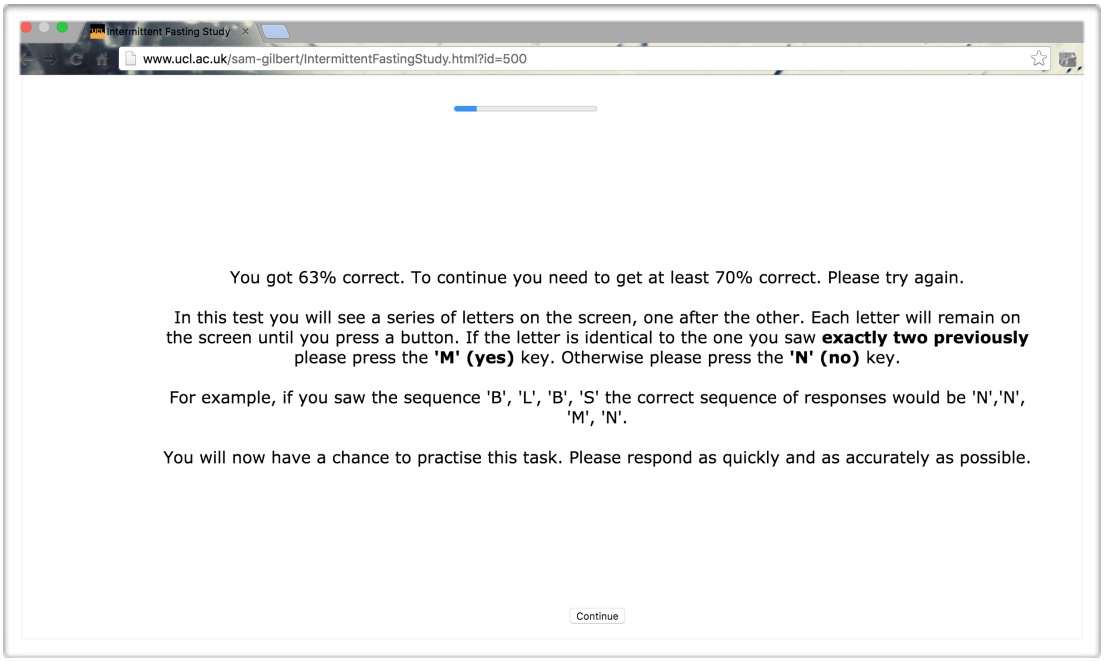


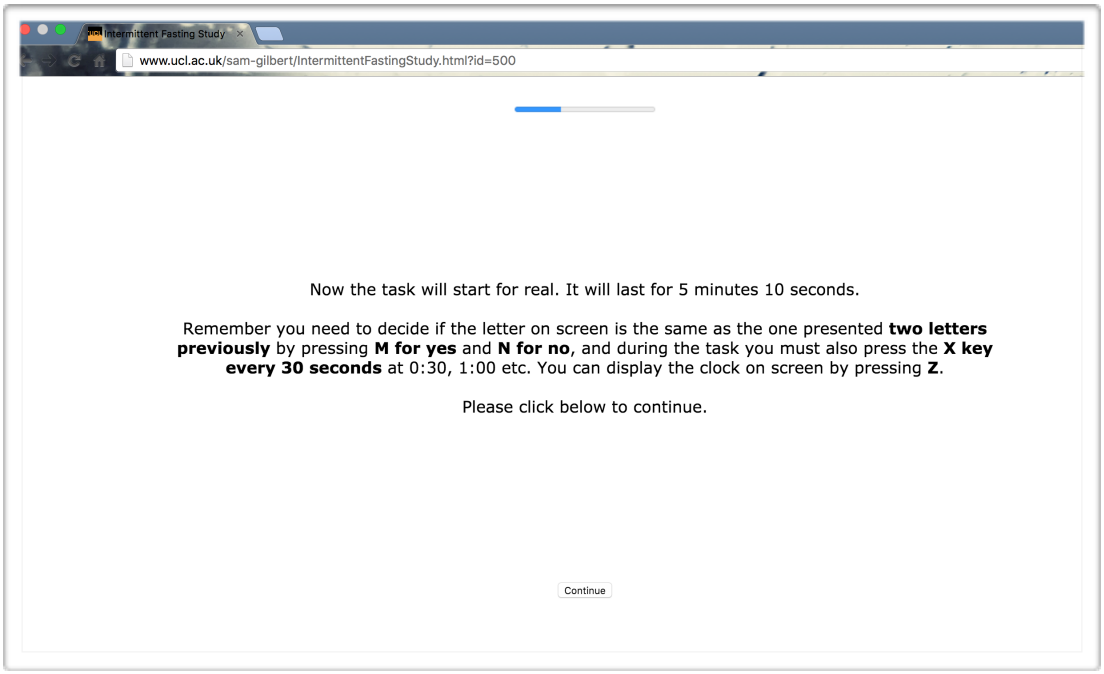
6. 2N-back task with inbuilt clock watching



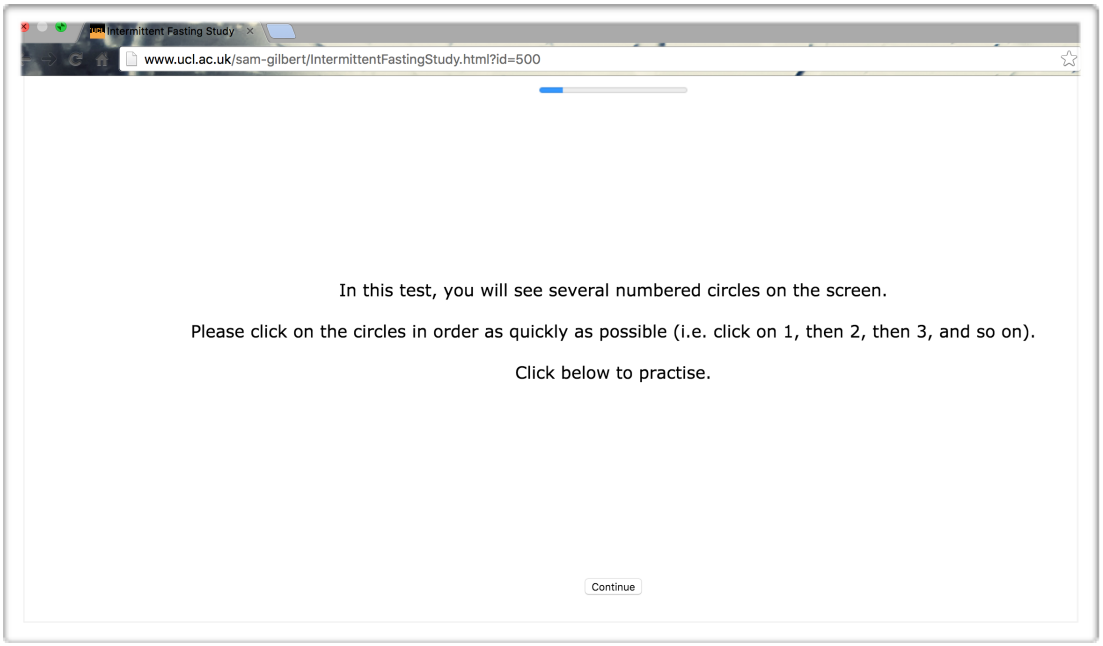

Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
H

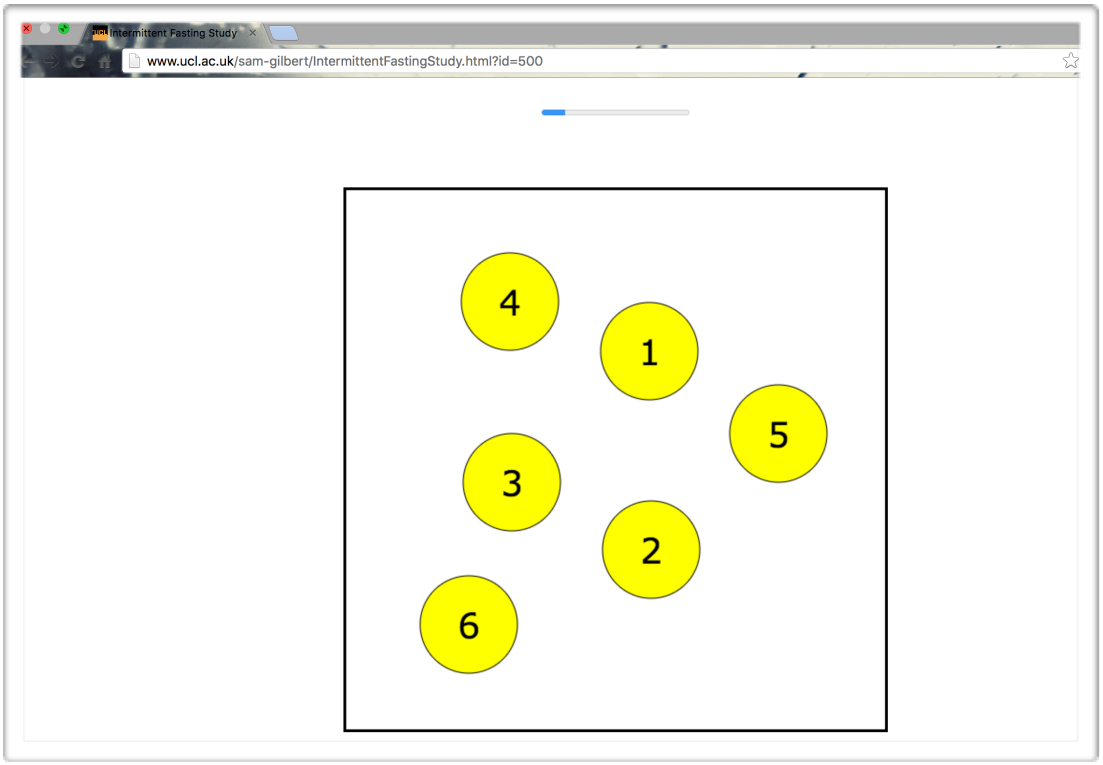

Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
In a moment, you will have another chance to pratise this task. Please continue just the same as before. But this time there will be one extra thing to do.
While you perform this task, there will be a clock running. You can see this clock whenever you like by pressing the 'Z' key. This will display the current time. Every 30 seconds (i.e. when the clock shows 0:30, 1:00, 1:30 etc.), please press the 'X' key. You need to press this key within 3 seconds of the correct time (e.g. between 0:27 and 0:33) so please press the 'X' key as close to the correct time as possible.
Please click below to practice the task. This time, the clock will start at 0:20 so you will need to press the 'X' key 10 seconds later. Remember, you can check the clock any time by pressing the 'Z' key.
Continue

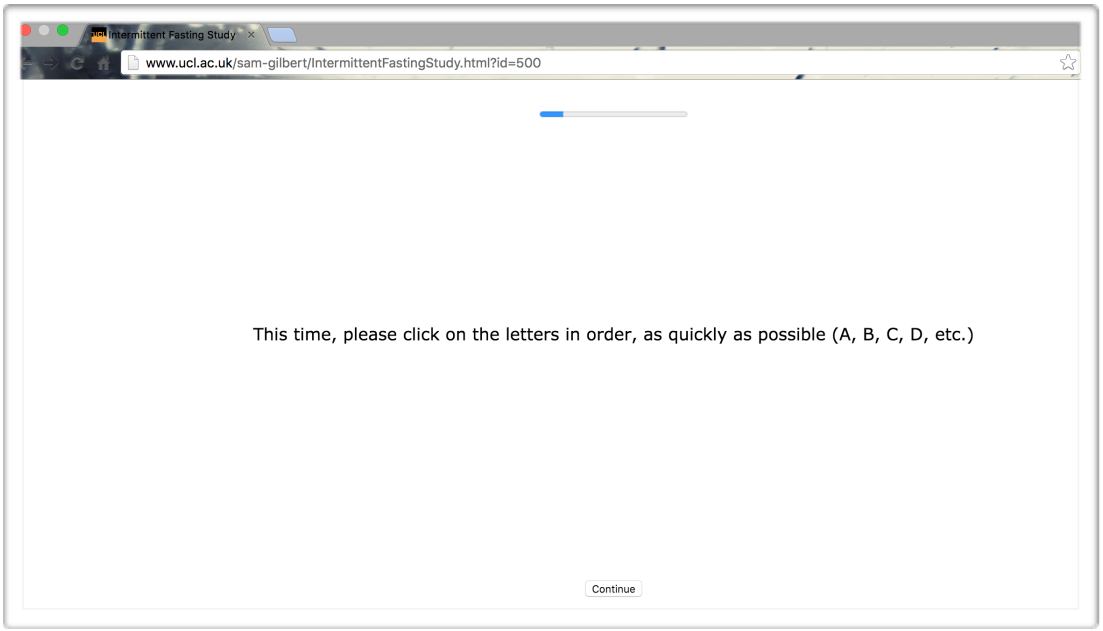

Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
You got 63% correct. To continue you need to get at least 70% correct. Please try again.
In this test you will see a series of letters on the screen, one after the other. Each letter will remain on the screen until you press a button. If the letter is identical to the one you saw exactly two previously please press the 'M' (yes) key. Otherwise please press the 'N' (no) key.
For example, if you saw the sequence 'B', 'L', 'B', 'S' the correct sequence of responses would be 'N','N', 'M', 'N'.
You will now have a chance to practise this task. Please respond as quickly and as accurately as possible.
Continue

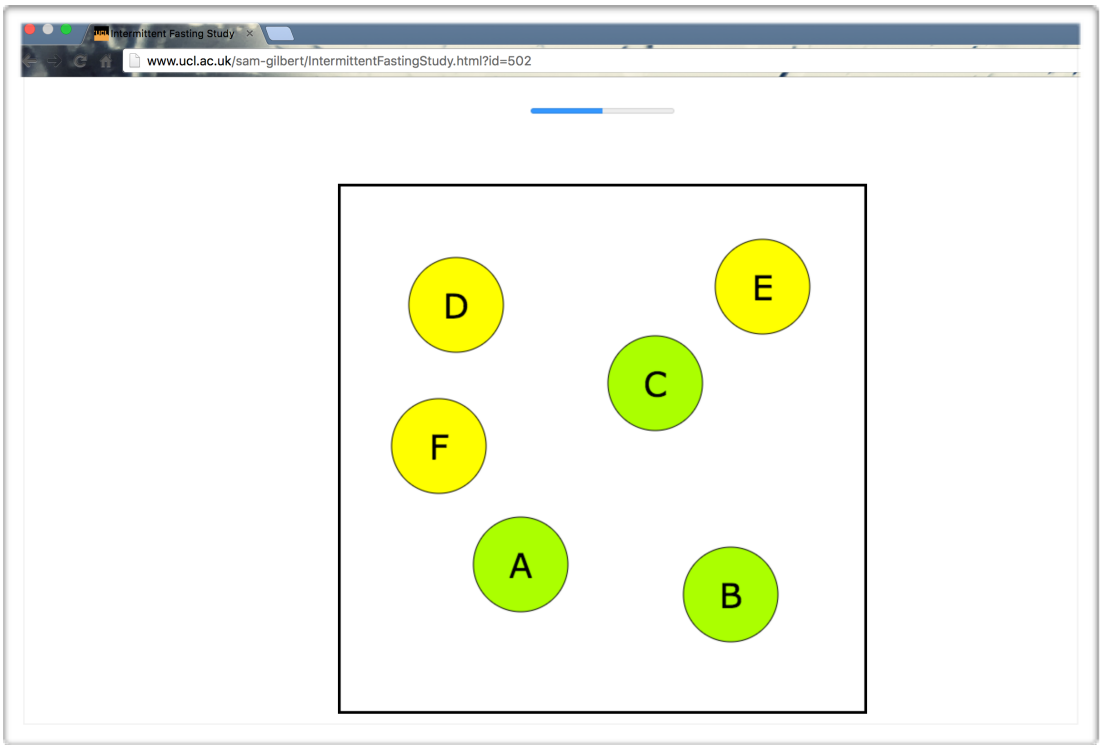

Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
Now the task will start for real. It will last for 5 minutes 10 seconds.
Remember you need to decide if the letter on screen is the same as the one presented two letters previously by pressing M for yes and N for no, and during the task you must also press the X key every 30 seconds at 0:30, 1:00 etc. You can display the clock on screen by pressing Z.
Please click below to continue.
Continue

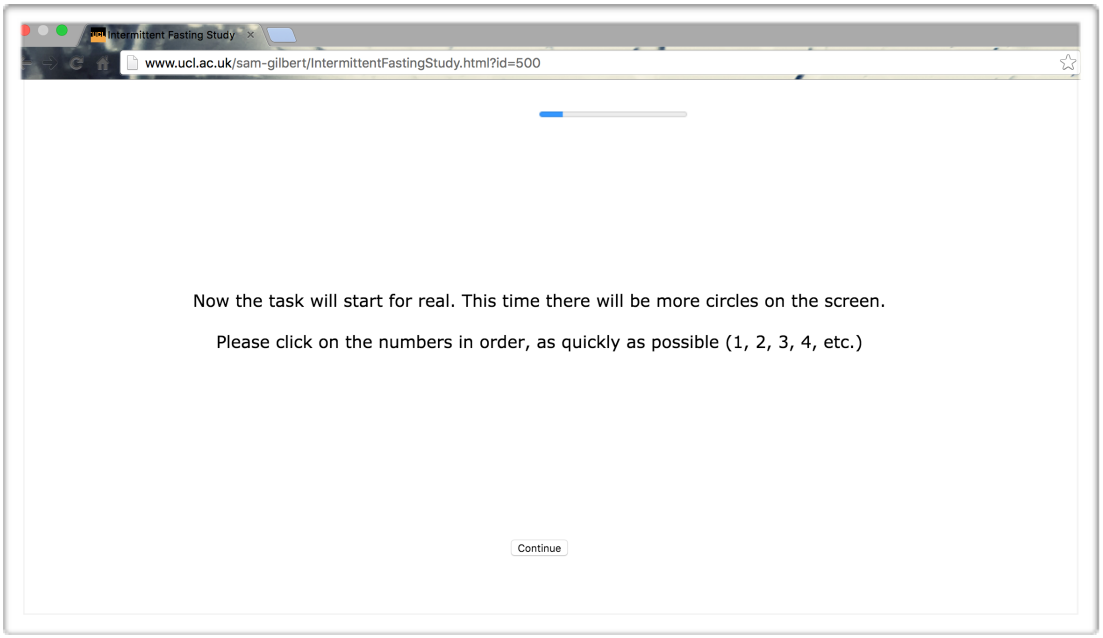
7. Trail making task - part a

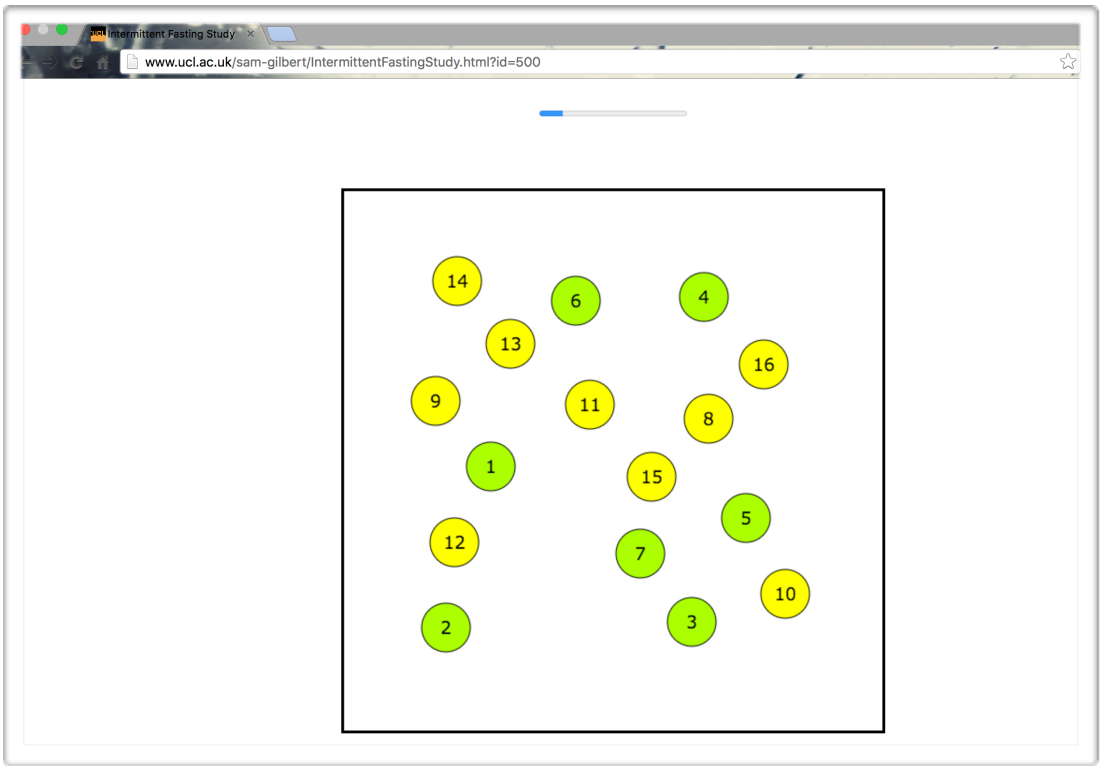





Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
This time, please click on the letters in order, as quickly as possible (A, B, C, D, etc.)
Continue


Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=502
D
E
C
F
A
B


Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
Now the task will start for real. This time there will be more circles on the screen.
Please click on the numbers in order, as quickly as possible (1, 2, 3, 4, etc.)
Continue


Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
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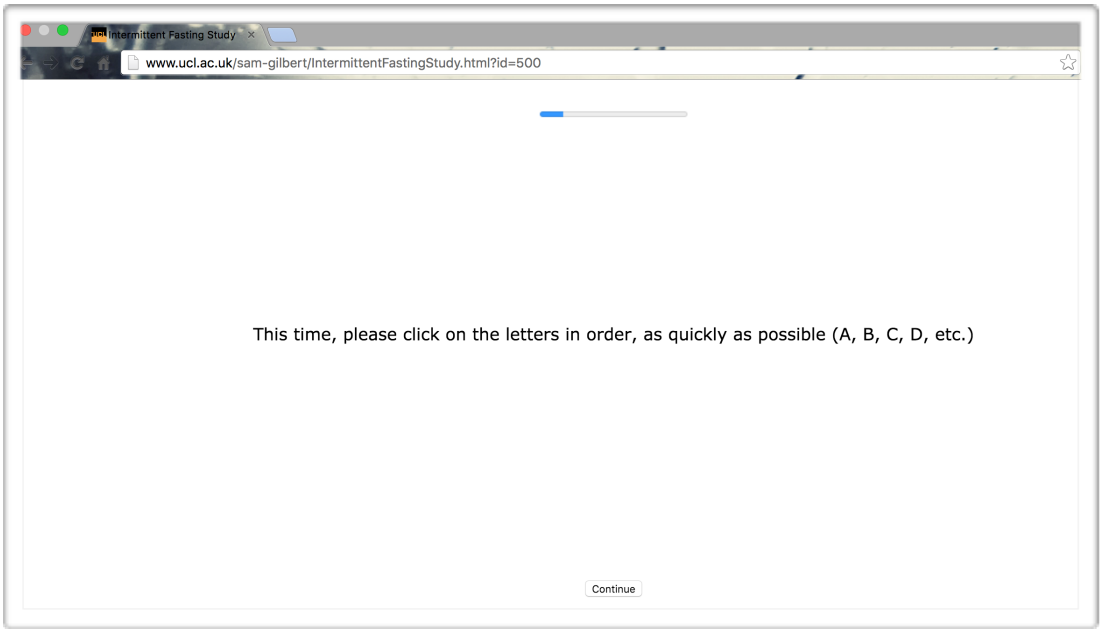
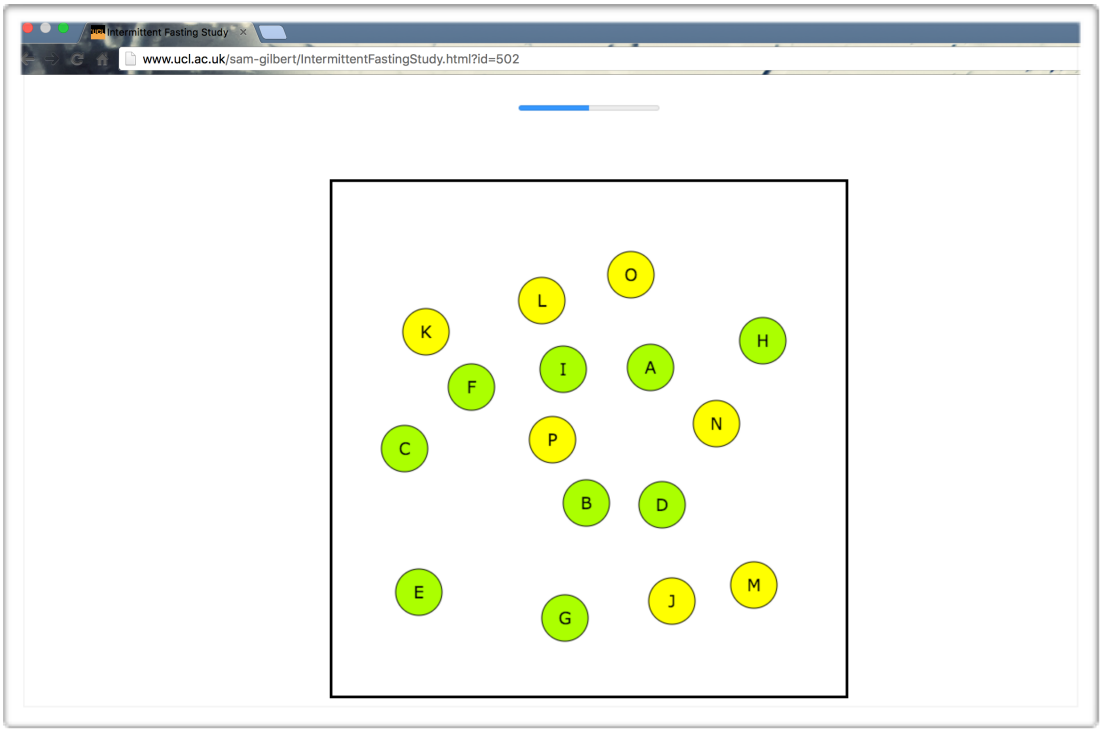
2
3


Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=500
This time, please click on the letters in order, as quickly as possible (A, B, C, D, etc.)
Continue


Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=502
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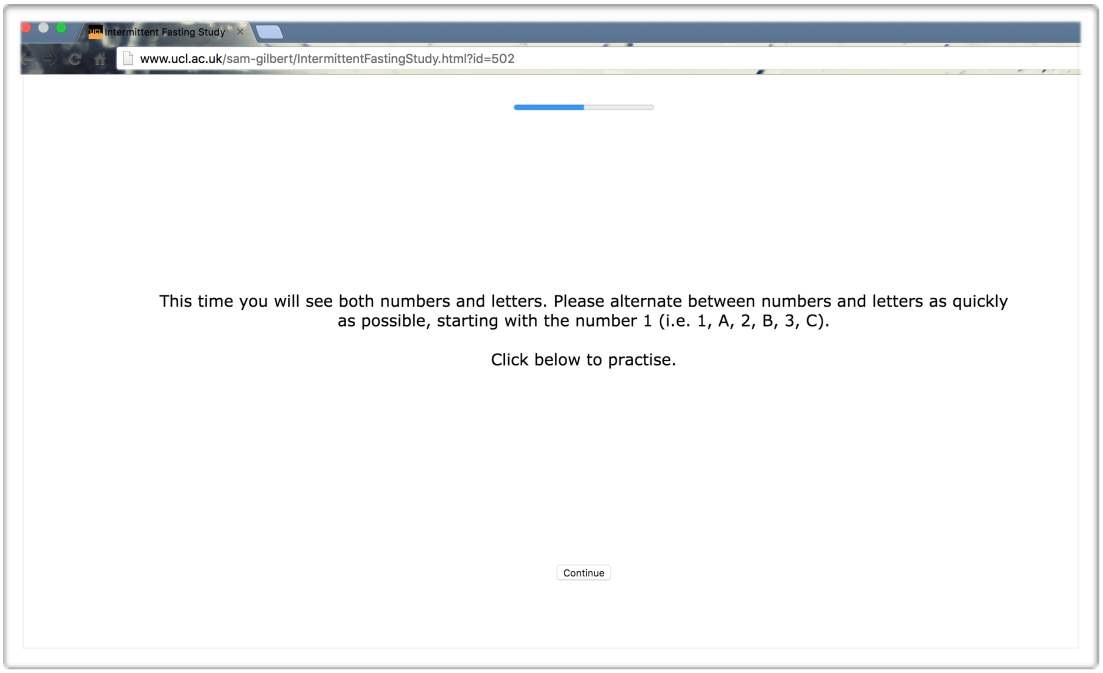
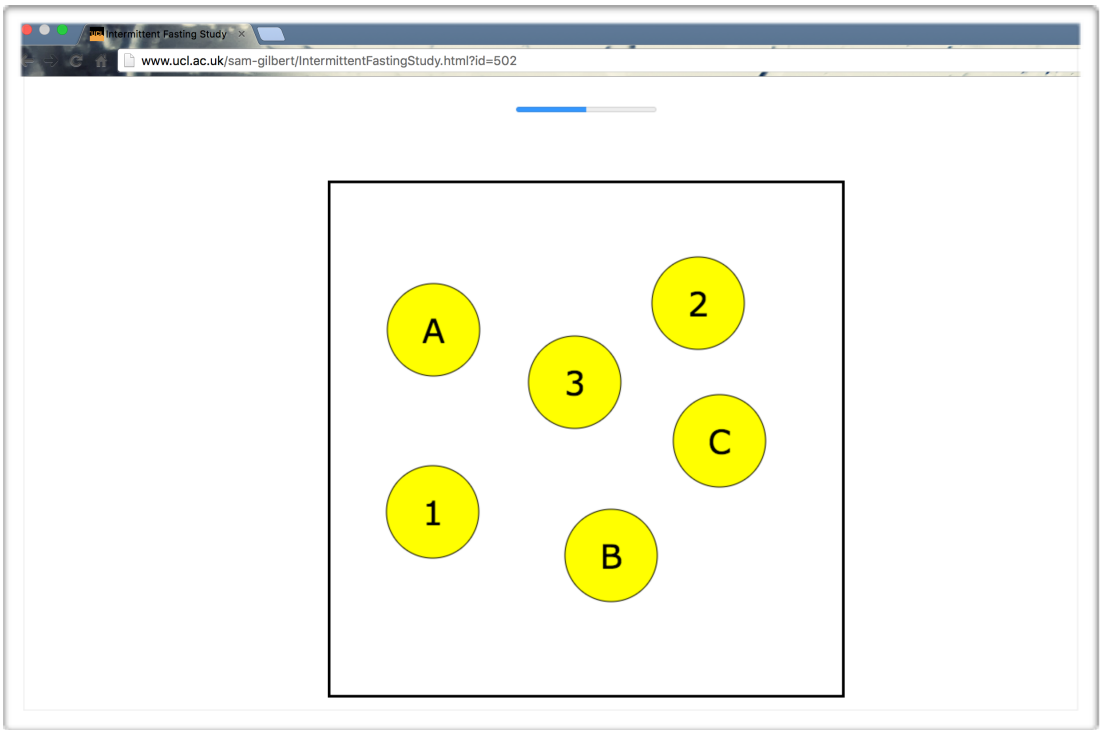
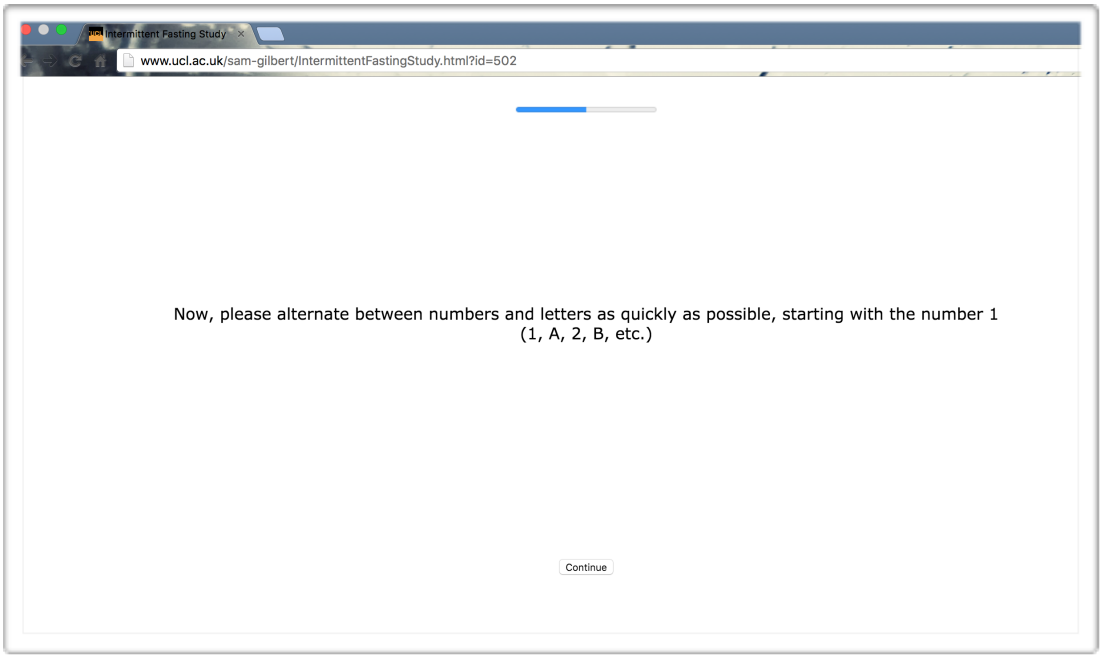
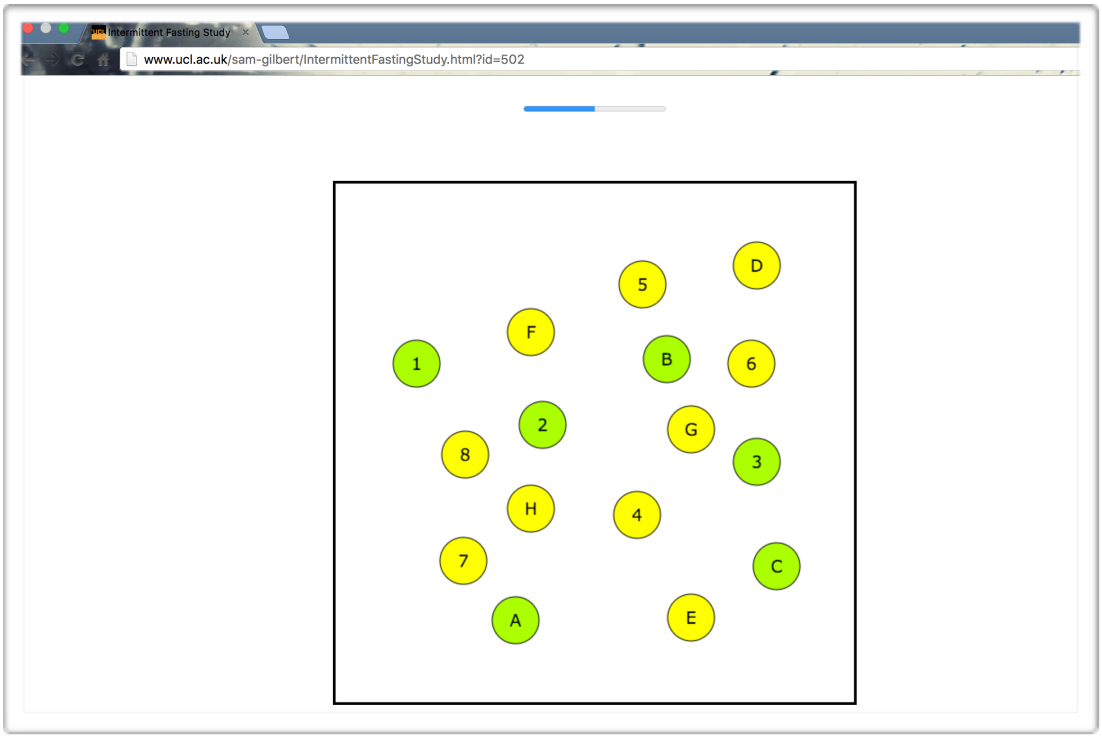
G

8. Trail making test - part B






Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=502
Now, please alternate between numbers and letters as quickly as possible, starting with the number 1
(1, A, 2, B, etc.)
Continue


Intermittent Fasting Study
www.ucl.ac.uk/sam-gilbert/IntermittentFastingStudy.html?id=502
D
5
F
1
B
6
2
G
8
3
H
4
7
C
A
E

Appendix XI

Correlational Matrices

Table A III

Correlational Matrix between Processing-Speed Tasks

		Tap Speed 1 - Fasting	Tap Speed 2 - Fasting	TMT A - Fasting	Tap Speed 1 - Non-Fasting	Tap Speed 2 -Non-Fasting	TMT A - Non-Fasting
Tap Speed 1 - Fasting	*r*	1	.799**	-0.061	.588**	.558**	-.266*
	p (two-tailed)		0.000	0.608	0.000	0.000	0.022
	N	74	74	74	74	74	74
Tap Speed 2 - Fasting	*r*		1	0.040	.453**	.488**	-0.066
	p (two-tailed)			0.735	0.000	0.000	0.577
	N		74	74	74	74	74
TMT A - Fasting	*r*			1	0.000	-0.036	.785**
	p (two-tailed)				0.999	0.761	0.000
	N			74	74	74	74
Tap Speed 1 - Non-Fasting	*r*				1	.946**	-0.116
	p (two-tailed)					0.000	0.326
	N				74	74	74
Tap Speed 2 -Non-Fasting	*r*					1	-0.116
	p (two-tailed)						0.327
	N					74	74
TMT A - Non-Fasting	*r*						1
	p (two-tailed)						
	N						74

****. Correlation is significant at the 0.01 level (2-tailed).**

***. Correlation is significant at the 0.05 level (2-tailed).**

Table A IV

Correlational Matrix Between Set-Shifting Tasks

		TMT set shifting - Fasting	TMT_setshifting - Non-Fasting	RC set shifting - Non-Fasting	RC_ set shifting - Fasting	RC set shifting Accuracy- Non-Fasting	RC set shifting Accuracy- Fasting
TMT_ setshifting - Fasting	*r*	1	.321**	0.127	0.127	0.050	-0.126
	p (two-tailed)		0.005	0.280	0.281	0.675	0.286
	N	74	74	74	74	74	74
TMT_ setshifting - Non-Fasting	*r*		1	0.077	0.123	0.196	0.050
	p (two-tailed)			0.513	0.295	0.094	0.673
	N		74	74	74	74	74
RC_ setshifting -Non-Fasting	*r*				.50	-0.0	0.1
	p (two-tailed)				0.0	0.8	0.1
	N						
RC_ setshifting - Fasting	*r*				1	0.141	0.164
	p (two-tailed)					0.231	0.163
	N				74	74	74
RC_ setshifting Accuracy- Non-Fasting	*r*					1	0.086
	p (two-tailed)						0.468
	N					74	74
RC_ setshiftingAccuracy - Fasting	*r*						1
	p (two-tailed)						
	N						74

**. Correlation is significant at the 0.01 level (2-tailed).